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Obesity in America

George A. Bray, M.D.
Editor

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8
115
79

CONTENTS

Page

Executive Summary and Preface v

Obesity in America: An Overview 1

Position Papers

1. Definitions, Criteria, and Prevalence of Obesity*
Ethan A. H. Sims 20

2. Pathogenesis of Obesity: Energy Intake and Expenditure*
Judith Rodin 37

3. Natural History of Obesity*
Lester B. Salans 69

4. Body Composition and the Natural History of Fatness**
Gilbert B. Forbes 95

5. Obesity: Its Risks and Hazards*
Alfred A. Rimm and Philip L. White 103

6. Physiological and Medical Concomitants of Obesity: The Framingham Study**
W. B. Kannel and Tavia Gordon 125

7. Conservative Approaches to Treatment*
Theodore B. Van Itallie 164

---

*Task Force report.

** Individually prepared report.

8. Treatment of Obesity with Drugs and Invasive Procedures*
George A. Bray 179

9. Obesity and the Social Environment: Current Status, Future Prospects*
Albert J. Stunkard 206

Appendix: Matrix for Action: Nutrition and Dietary Practices*
Jane E. Fullarton 241

References 265

Task Forces 273

Conference Participants 275

Index 282

Executive Summary and Preface

Obesity and its attendant problems have long been a matter of concern to both the medical community and the public. The Fogarty International Center (FIC) conference on obesity held at the National Institutes of Health in October 1977 in response to this concern was timely, for it served to stimulate official action on a growing problem of illness and deaths associated with liquid protein diets.

At the first FIC obesity conference 4 years earlier, health professionals from six countries presented papers which later were compiled into a thorough state-of-the-art review of current medical knowledge on the problem (19).

The second conference involved 91 professionals in political and behavioral sciences and in biomedicine, who assembled from 13 countries to prepare an updated review of scientific knowledge on obesity, to evaluate recent research results, and to develop recommendations for the prevention and management of obesity. The format for the 1977 conference differed from that of the earlier meeting. Several task forces were organized for an indepth study of nine major topics related to the conference theme. Reports from these groups, rather than individual papers, were presented at the conference and were modified following discussion by the participants. This report presents the resulting consensus on the state of research in obesity. Recommendations for action are presented in the overview.

The first logical step in developing such recommendations was to define the problem. This was addressed by the Task Force on the Definitions, Criteria, and Prevalence of Obesity, which concluded that there currently exist no entirely satisfactory standards by which to define or to measure obesity. That report draws a distinction between obesity, which refers to a surplus of fat, and overweight, which refers to an excess of body weight relative to height. The report further recommends that a proper consideration of obesity should recognize the condition as a group of related disorders and should take into account different types of obesity, such as childhood-onset, and adult-onset, and identify different anatomical sites of fat deposition. Because of the epidemic proportion of obesity, the task force stressed the importance of proceeding with action and suggested that long-term epidemiologic studies into the cultural and socioeconomic distribution of obesity might offer insights into its basic causes.

That obesity results from the ingestion of more fuel (i.e., food) than an individual expends is widely understood; that the mechanisms controlling intake and expenditure of food energy are not understood was the conclusion of the Task Force on the Pathogenesis of Obesity: Energy Intake and Expenditure. It was formerly believed that a lateral hypothalamic "feeding center" was responsible for the initiation of eating and a ventromedial hypothalamic "satiety center" for its termination; but, the task force reports, recent research has disproved that theory. No one has yet arrived at an acceptable alternative explanation. In addition to discussing the physiologic influences on eating--including hypothalamic, neuroendocrine, neural, hormonal, and hepatic--the task force reviewed several social factors that play a dramatically important role in developing eating habits. Social factors are also important in determining an individual's pattern of exercise; but exercise itself, the report stated, is not the main factor determining energy expenditure. The task force cited evidence that metabolic processes are influenced by specific types of exercise and diet and that individuals do not use energy at a constant rate. This task force concluded that further research is needed.

The report of the Task Force on the Natural History of Obesity included a detailed comparison of different methods for quantitating body fat and suggested that measurements of skinfold thickness may offer the most practical index. However, once the measurement has been established, the report notes, there still exists the problem of interpretation: no one knows how much body fat is normal or desirable. Reviewing recent studies of obesity in human beings and animals, the task force report stated that, although it has been widely accepted that massive, early-onset obesity is more resistant to therapy than mild, adult-onset obesity, this conclusion has not yet been adequately documented. The document also reports the discussion on the relationship between obesity and insulin metabolism, and between hyperlipoproteinemia and hypercholesterolemia, concluding that further research in these areas is required.

Body composition analysis is offered as one possible approach to the definition of obesity in the paper on Body Composition and the Natural History of Fatness. The report traces the wide differences in body composition based on age and sex and states that "the final answer (to the definition and measurement of obesity) is the product of the number of adipocytes per unit weight of fat and total body fat." The paper further points out that obese children tend to show accelerated growth and that obese persons generally have a larger lean body mass than do lean persons of the same height, sex, and age.

Further research is needed into the risks, hazards, and disadvantages of obesity, according to the task force studying that subject, even though this area has been widely documented. The task force evaluation suggests that obesity is related to or associated with the following conditions: hypertension, diabetes mellitus, gout, heart size and function, menstrual and ovarian abnormalities, endometrial carcinoma, atherosclerosis, gallbladder disease, and various psychological and social handicaps. To collect long-term information on the relationship between obesity and these conditions and on the problem of obesity itself, the task force recommended establishing a National Obesity Register to follow obese individuals over a span of years and to maintain a pool of current information for use by researchers. Among the areas that need further investigation, the report pinpoints several questions, including whether obesity is specifically related to sudden death and congestive heart failure, and whether obesity affects survival after a heart attack.

One long-term, broad scale health investigation is the Framingham (Massachusetts) Study of some 5,209 men and women. Selected data from the study, which are included in this report, indicate that coronary heart disease would be reduced by 25 percent and congestive heart failure by 35 percent if everyone in the United States were at optimal weight. This goal requires a complete change in the Nation's habits and seems a manifestly difficult undertaking: difficult, but not impossible, as the recommendations included herein attest.

Two groups addressed the question of how to treat obesity: the Task Force on Conservative Approaches to Treatment, and the Task Force on Treatment of Obesity with Drugs and Invasive Procedures. The conservative approaches discussed include total fasting, recommended only for a very few selected patients; protein-supplemented fasting, which has had success in some patients but carries the stigma of the poorly understood events surrounding the deaths of some individuals who used the liquid protein diets; low-calorie balanced diets; exercise regimens; behavioral therapy; and community-based programs. Clearly, the hazards of each of these treatments vary. The task force points out that these treatments have uneven success rates; each works for some patients, but none works for all.

The more extreme therapies discussed included both pharmacologic treatments and surgical approaches, including intestinal bypass, gastric bypass, acupuncture, and jaw wiring. Again, these treatments carry varying degrees of risk and of success; and, the task force concluded, it is necessary to balance the risk of obesity with the risk of treatment.

The Task Force on Proposals for Public Action also addressed the question of treatment, suggesting that behavioral therapies hold promise for future treatment of obesity in both small- and large-scale programs. Stressing that obesity is largely a result of lifestyle, the task force report predicted that leadership efforts to control obesity will pass from the medical field to nonmedical areas: business and industry, the communications media, the education system, government, and volunteer agencies. The report states that a combination of approaches from each of these areas will offer the most effective form of obesity control.

Additional information that became available between the time of the conference in October 1977 and the completion of this report has been included in the overview. Among these additions are the newer data from the Life Insurance Study of 1979, which were provided through the kindness of Mr. Edward Lew, a participant in the conference. Additional data on the prevalence of obesity in 1960-62 and 1971-74 were calculated by Mr. Sidney Abraham of the National Center for Health Statistics. These additions address some of the questions raised by gaps in our knowledge at the time of the conference.

This conference on obesity was planned by a small working group including Drs. George Cahill, Theodore Van Itallie, Ethan Sims, Judith Rodin, Jules Hirsch, Philip White, Albert J. Stunkard, Aaron Altschul, Johanna Dwyer, and Lester B. Salans. Without the help of each of these individuals in developing and editing task force reports there would never have been a conference. Preparation of the final document was the work of several people. Ms. Ann Mannheimer used her editorial skill to improve the readability of all the reports and prepared the executive summary. The contribution of the Fogarty International Center staff in handling the conference and in managing the publication of this report was essential to the success of this project.

George A. Bray, M.D.
Conference Chairman

August 1, 1979

Obesity in America: An Overview

"We are unanimous in our belief that obesity is a hazard to health and a detriment to well-being. It is common enough to constitute one of the most important medical and public health problems of our time, whether we judge importance by shorter expectation of life, increased morbidity, or cost to the community in terms of money and anxiety"(88). The sentiments expressed in this quotation from our British colleagues succinctly summarize the feeling of the conference on Obesity in America. This conference, held at the National Institutes of Health in October 1977, was centered around nine task force reports which examined the many issues surrounding obesity. The task force reports, a summary of their findings, and specific recommendations make up the bulk of this report. This brief summary presents the pertinent features of the problem as given in the task force reports, as well as the key findings and their implications.

Two events, a decade apart, highlight the hazards associated with treatment for obesity and indicate the potential consequences of allowing a problem so important and pervasive to receive so little attention. In 1978, the diet pill industry hearings of the United States Senate, chaired by the late Senator Philip Hart, focused on deaths associated with the use of appetite-suppressing drugs in combination with other agents for the treatment of obesity (150). The outcry from these hearings resulted in stiffened Federal regulations for the prescription of amphetamines and similar drugs. However, no additional support was forthcoming for the evaluation and assessment of treatment programs for obesity or for exploring the underlying causes of obesity, and public interest soon returned to its ever-present, often expensive, search for ways to be thin. In 1977, at the time of the conference on Obesity in America, we were once again in the midst of a rash of deaths--this time associated with the use of protein-supplemented fasts, a new form of treatment for obesity. According to the Center for Disease Control in Atlanta, more than 15 deaths were associated with the use of various commercial preparations of protein hydrolysates as a diet supplement in individuals with no apparent disorder other than obesity (54, 112, 113). In assessing these data, three serious deficiencies became apparent:

- There are few adequate programs for assessing, developing, and testing new treatments prior to general use in obese patients.
- There is a lack of information about programs for treatment of overweight, even though its relative hazards have been amply documented over a period of 75 years.
- The search for slimness is especially common among women, where information is often most deficient.

The definition and prevalence of obesity were addressed by one of the nine task forces, the Task Force on the Definitions, Criteria, and Prevalence of Obesity. Obesity refers to a surplus in body fat. Overweight, on the other hand, refers to an excess in body weight relative to standards for height. For most situations, overweight and obesity are used synonymously, although they are not identical. This task force stressed the need for improved ways to classify and subdivide groups of obese people, but the problem of defining precisely what is meant by obesity proved difficult. With this difficulty in mind, we can make the following statements based on data obtained from the Health and Nutrition Examination Survey I conducted by the National Center for Health Statistics (figure 1).[1]

- A higher proportion of women than men are obese.

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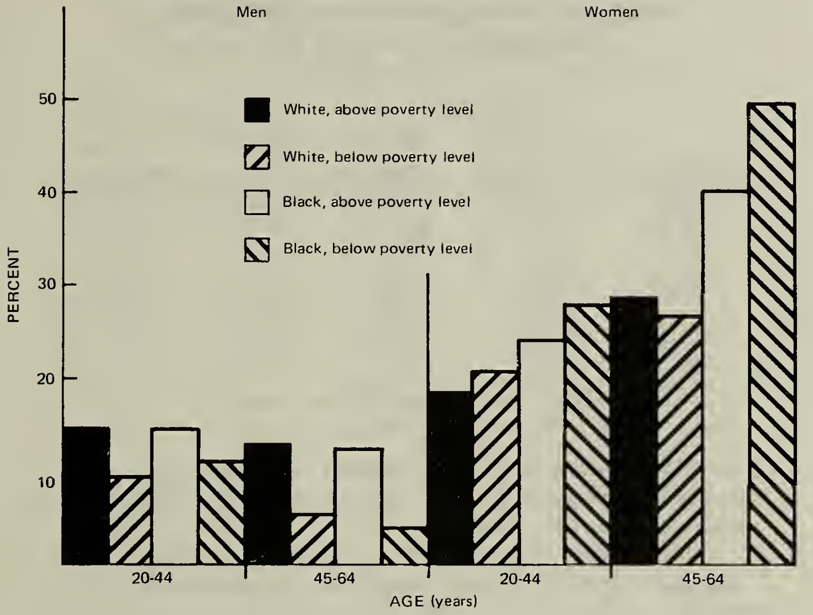
[1] Obesity measure is based on triceps skinfold measurement and is defined as greater than the sex-specific 85th percentile measurements for persons ages 20-29.

FIGURE 1.--Obesity among persons ages 20-74 according to sex, age, and poverty level: United States, 1971-74.



NOTE.--Obesity measure is based on triceps skinfold measurements and is defined as greater than the sex-specific 85th percentile measurements for persons ages 20-29.

[Source: Health, United States, 1978. Third Annual Report on the Health Status of the Nation, Hyattsville, Md.: U.S. Government Printing Office, DHEW Publication No. (PHS) 78-1232. December 1978. Table 43, page 215.]

- Black women are more likely to be obese than white women, regardless of age or income level.
- Among people ages 45-64 whose incomes are below the poverty level,
  - 49 percent of black women and 26 percent of white women are obese;
  - 4 percent of black men and 5 percent of white men are obese.
- Among people ages 45-64 whose incomes are above the poverty level,

TABLE 1.--Prevalence of overweight. Percent of population deviating by 10-19 percent and by 20 percent or more from desirable weight:[a] United States, Health and Nutrition Examination Survey, 1971-74

	Men		Women	
Age	10-19%	20% or more	10-19%	20% or more
20-74	18.1%	14.0%	12.6%	23.8%
20-24	11.1	7.4	9.8	9.6
25-34	16.7	13.6	8.1	17.1
35-44	22.1	17.0	12.3	24.3
45-54	19.9	15.8	15.1	27.8
55-64	18.9	15.1	15.5	34.7
65-74	19.1	13.4	17.5	31.5

[a] Estimated from regression equations of weight on height for men and women ages 20-29 years, obtained from HANES I.

[National Center for Health Statistics. S. Abraham and C. L. Johnson, "Overweight Adults 20-74 Years of Age: United States, 1971-74." Vital and Health Statistics. Advance Data No. 51. Hyattsville, Md.: Public Health Service, DHEW. In preparation.]

-- 40 percent of black women and 28 percent of white women are obese;

-- 12 percent of black men and 13 percent of white men are obese.

- In the 20-74 age range, 14 percent of the men and 24 percent of the women are 20 percent or more overweight (table 1).
- A higher percentage of men than women are 10-19 percent overweight, but the reverse is true in the case of those 20 percent or more overweight.
- The percentage of women and men ages 25-44 who are 20 percent or more overweight was higher in 1971-74 than in 1961-62 (table 2).
- A smaller percentage of older women ages 65-74 were overweight in 1971-74 than in 1961-62 (table 2).

TABLE 2.--Prevalence of overweight. Percent of population deviating by 20 percent or more from desirable weight:[a] United States, Health Examination Survey 1960-62 and Health and Nutrition Examination Survey 1971-74

	Men		Women	
Age	1960-62	1971-74	1960-62	1971-74
20-74	14.5%	14.0%	25.1%	23.8%
20-24	9.6	7.4	9.1	9.6
25-34	13.3	13.6	14.8	17.1
35-44	14.9	17.0	23.2	24.3
45-54	16.7	15.8	28.9	27.8
55-64	15.8	15.1	38.6	34.7
65-74	14.6	13.4	38.8	31.5

[a] Estimated from regression equation of weight on height for men and women ages 20-29 years, obtained from HANES I.

[National Center for Health Statistics. S. Abraham and C. L. Johnson, "Overweight Adults 20-74 Years of Age: United States, 1971-74." Vital and Health Statistics. Advance Data No. 51. Hyattsville, Md.: Public Health Service, DHEW. In preparation.]

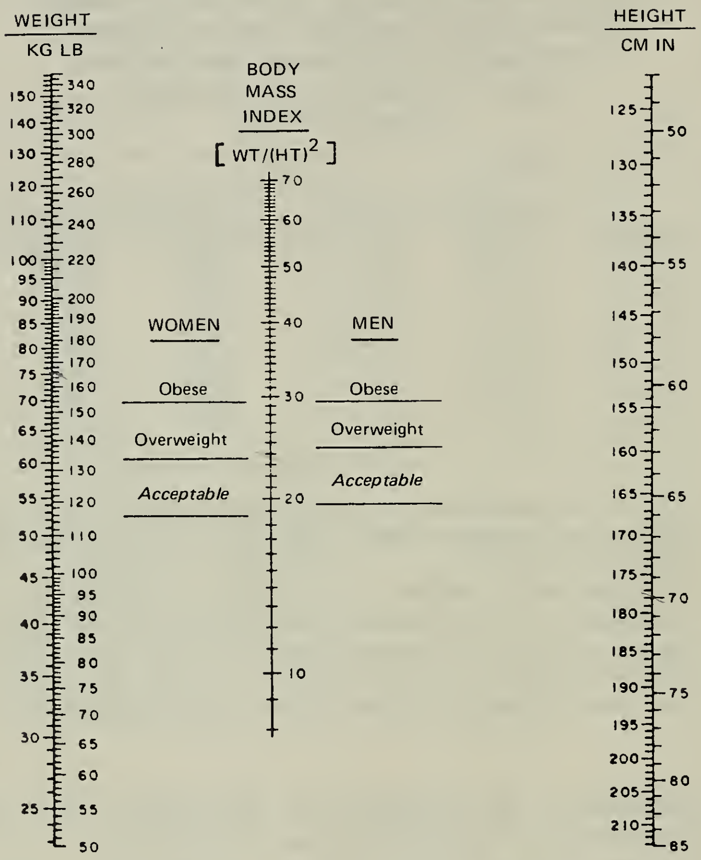
Based on the findings of this task force, two recommendations were made:

- Evaluation of relative weight for clinical purposes should be based on the Fogarty Center Table (table 3) [16(1):72], which is an adaptation of the Metropolitan Life Insurance table.
- Investigators should consider using the body mass index as a method of relating variations in weight to height (figure 2) and consider more specific means of assessing body fat and its distribution, particularly when such data may affect interpretation of the results (18).

Deficiencies identified by this task force pointed up the need for several research programs:

- Improvement of methods for quantitating body fat.

FIGURE 2.--Nomogram for body mass index.



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- More thorough calibration of existing methods of quantitation before application to all segments of the population.
- Development of new methods for classifying obesity, and more studies to determine which particular types of obesity may lead to greater risk of developing associated disorders such as diabetes, hypertension, and hyperlipidemia.
- Development of techniques for identifying individuals at risk for obesity.
- Additional information concerning factors associated with the development of obesity.

TABLE 3.--Guidelines for body weight

Metric

	Men			Women		
	Weight (kg)[a]			Weight (kg)[a]		
Height[a] (m)	Average	Acceptable weight		Average	Acceptable weight	
1.45				4.60	42	53
1.48				46.5	42	54
1.50				47.0	43	55
1.52				48.5	44	57
1.54				49.5	44	58
1.56				50.4	45	58
1.58	55.8	51	64	51.3	46	59
1.60	57.6	52	65	52.6	48	61
1.62	58.6	53	66	54.0	49	62
1.64	59.6	54	67	55.4	50	64
1.66	60.6	55	69	56.8	51	65
1.68	61.7	56	71	58.1	52	66
1.70	63.5	58	73	60.0	53	67
1.72	65.0	59	74	61.3	55	69
1.74	66.5	60	75	62.6	56	70
1.76	68.0	62	77	64.0	58	72
1.78	69.4	64	79	65.3	59	74
1.80	71.0	65	80			
1.82	72.6	66	82			
1.84	74.2	67	84			
1.86	75.8	69	86			
1.88	77.6	71	88			
1.90	79.3	73	90			
1.92	81.0	75	93			

Nonmetric

	Men			Women		
	Weight (lb)[a]			Weight (lb)[a]		
Height[a] (ft, in)	Average	Acceptable weight		Average	Acceptable weight	
4 10				102	92	119
4 11				104	94	122
5 0				107	96	125
5 1				110	99	128
5 2	123	112	141	113	102	131
5 3	127	115	144	116	105	134
5 4	130	118	148	120	108	138
5 5	133	121	152	123	111	142
5 6	136	124	156	128	114	146
5 7	140	128	161	132	118	150
5 8	145	132	166	136	122	154
5 9	149	136	170	140	126	158
5 10	153	140	174	144	130	163
5 11	158	144	179	148	134	168
6 0	162	148	184	152	138	173
6 1	166	152	189			
6 2	171	156	194			
6 3	176	160	199			
6 4	181	164	204			

[a] Height without shoes, weight without clothes.

Adapted from the recommendations of the Fogarty Center conference on obesity, 1973.

The Task Force on the Risks, Hazards, and Disadvantages of Obesity suggested possible hazards of obesity from a medical and a social point of view:

- Increased risk of cardiovascular disease, particularly sudden death.
- Relation to the onset of hypertension. The prevalence of hypertension may be increased three to five times in individuals who are 50 percent or more above desirable weight.
- Increased risk of developing gallbladder disease.
- Increased risk of developing non-insulin-dependent (usually maturity-onset) diabetes mellitus.
- Increased risk of developing endometrial carcinoma.
- Aggravation of degenerative joint diseases.
- Economic and social handicap.

The quantitative relationships between obesity and other conditions may be modified by many factors, including the magnitude of excess weight, the individual's age, the distribution of body fat, and the age at which overweight begins. The relationship of excess weight to the risk of mortality is shown in table 4. This information was obtained from the most recent life insurance data and from an independent study conducted by the American Cancer Society. In both cases, the extra risk to life increased as the degree of overweight increased. Thus, from our present information, significant health risks are associated with obesity, particularly when it is of major proportion. Obesity acquired in adult years may carry a greater toll in terms of cardiovascular and metabolic derangements than does lifelong obesity of moderate severity.

Weight loss may reduce these risk factors. Significant weight reduction lowers blood pressure, blood cholesterol, and blood glucose, as well as uric acid and triglyceride concentrations, and may be related to a lower risk of developing cardiovascular disease and diabetes mellitus. From the data collected in Framingham, Massachusetts, it is estimated that "if everyone were at optimal weight, there would be 25

TABLE 4.--Mortality experience in relation to deviation from average weight

Mortality ratio relative to standard experience

	Men		
Deviation from average weight (%)	Insured lives		General population
	1954-72[a] (provisional)	1935-54[b]	1959-72[c]
-20	105	90	110
-10	94	95	100
+10	111	113	107
+20	120	125	121
+30	133	142	137
+40	150	167	162
+50	171	200	210
+60	195	260	--

	Women		
Deviation from average weight (%)	Insured lives		General population
	1954-72[a] (provisional)	1935-54[b]	1959-72[c]
-20	110	99	100
-10	97	95	95
+10	106	109	108
+20	110	121	123
+30	125	130	138
+40	136	--	162
+50	150	--	200
+60	--	--	--

[a] Society of Actuaries and Association Life Insurance Medical Directors, Build and Blood Pressure Study, 1979.

[b] Society of Actuaries and Association Life Insurance Medical Directors, Build and Blood Pressure Study, 1959.

[c] American Cancer Society, Cancer Prevention Study.

percent less coronary heart disease, and 35 percent less congestive heart failure and brain infarction" (93).

This task force identified three important gaps in knowledge for which additional research is needed:

- Most of the data about risk are based on very simple measures of obesity, such as relative weight. To provide more useful data conforming to the concept that obesity is a symptom of many underlying conditions, a significant effort is needed to obtain long-term data employing more sophisticated indexes of fatness, with attention to the natural history of possible subgroups of obesity.
- Information about risks associated with massive obesity is limited. Special subsections of the population in which this is a high-risk problem need to be identified, and the risks associated with obesity and other factors need to be identified and segregated (1).
- The relative importance of obesity in the presence and absence of other risk factors, such as smoking, needs to be quantified and the results made available to the public for use in planning approaches to the treatment of obesity through appropriate changes in diet and physical activity.

Task forces on the Natural History of Obesity and on the Pathogenesis of Obesity: Energy Intake and Expenditure, which dealt with the development of obesity and its natural history, focused on information available from studies on food intake, energy expenditure, and the cellular tissue in which fat is stored. They concluded that large and significant gaps remain in our understanding of why obesity develops. Recent data on median caloric intake based on the Health and Nutrition Examination Survey (table 5) suggest that low levels of energy intake may be more common than previously thought (115). It is clear that obesity results either from ingestion of more food energy than the body needs or utilizes, or from the expenditure of less energy than normal. Therefore, it is obvious that prevention of weight gain during adult life requires careful individual attention to food intake and physical activity. These simple dictums, however, are compounded by difficulties in adequately quantitating energy intake and output.

TABLE 5.--Median caloric intake values for persons ages 1-74 years, by sex, age, and race: United States, 1971-74[a]

Age (yrs)	Men		Women	
	White	Black	White	Black
1	1,282	1,146	1,162	1,182
2-3	1,504	1,379	1,340	1,360
4-5	1,721	1,647	1,548	1,594
6-7	2,023	1,769	1,784	1,692
8-9	2,097	1,902	1,833	1,645
10-11	2,180	1,877	1,885	1,846
12-14	2,441	2,161	1,858	1,731
15-17	2,890	2,311	1,635	1,601
18-19	2,911	2,482	1,601	1,498
20-24	2,792	2,188	1,580	1,619
25-34	2,591	2,658	1,559	1,352
35-44	2,443	2,144	1,512	1,324
45-54	2,244	1,929	1,465	1,178
55-64	1,988	1,633	1,331	1,156
>65	1,718	1,439	1,254	1,104

[a] Obesity measure is based on triceps skinfold measurement and is defined as greater than the sex-specific 85th percentile measurements for persons ages 20-29 years.

[National Center for Health Statistics. S. Abraham, M. D. Carroll, C. M. Dresser, and C. L. Johnson, "Dietary Intake Source Data." Vital and Health Statistics. Hyattsville, Md.: DHEW Publication No. (PHS) 79-1221. In preparation.]

Major gaps in knowledge identified by these task forces can be summarized under three headings:

- Inadequate understanding of factors that control the start of a meal, what and how much is eaten, and how meals are terminated.
- Inadequate understanding of the relation of physical activity to food intake and obesity.
- Inadequate understanding of the factors controlling lipid metabolism, intermediary metabolism,

and the development and function of fat cells in relation to energy input and expenditure.

Two task forces, one on Conservative Approaches to Treatment and the other on Treatment of Obesity with Drugs and Invasive Procedures, focused on treatment for obesity. The treatments which are now available include 1) many kinds of calorie restricted diets; 2) total starvation, or zero-calorie diet; 3) fasts supplemented with natural protein or protein plus carbohydrate; 4) behavioral techniques; 5) self-help groups that may use one or more of the preceding modalities; 6) pharmacologic agents; 7) jaw wiring; 8) acupuncture; and 9) surgical intervention.

The risk of treatment clearly varies with the type of treatment. Since the risks associated with being overweight can vary markedly, it is necessary to balance them with the relative risks of the contemplated treatment.

Techniques for predicting success or failure of weight loss are poor. All treatment programs have been successful for some individuals and unsuccessful for others. At present, however, there are no generally recognized techniques for predicting a priori which individuals will be successful and by which method. This deficiency reflects the inadequacy of the tools for making this assessment and may also reflect our inadequacies in identifying different types of obesity and the different mechanisms by which intervention can cause weight loss. The desirability of selecting the most suitable technique beforehand makes the development of methods of predicting success a matter of highest priority.

The results of dietary, behavioral, and pharmacologic treatment have often been discouraging. The percentage of patients maintaining long-term weight loss after a course of treatment is small, ranging from 5-25 percent. Thus, 75-95 percent regain some or all of the weight which they have lost. There is a major concern over whether it is better to lose weight and regain it in a cyclic fashion or to stay moderately obese through the same period of time. For many people, the frustrations of cycling through weight loss and gain may be more detrimental than the health hazards of remaining moderately, but stably, overweight. This problem represents a major gap in our knowledge.

Three other task forces examined the current state of basic research (the Task Force on Priorities for Basic Research) and clinical research (the Task Force on Priorities for Clinical Research), identifying the gaps in knowledge and assessing some of the policy implications (the Task Force on Proposals for Public Action).

Recommendations for Action

Obesity is a problem of society as well as a problem of the individual. For most people, obesity is not solely a medical or nutritional problem or one of genetic susceptibility. It is also a problem of lifestyle, of patterns of eating and physical activity, of prevailing notions about what is good and what is desirable; it is subject to firmly established cultural patterns and powerful social and economic forces.

These social and economic forces do not act in a uniform manner; obesity is not evenly distributed in the population. Upper socioeconomic groups have already made great headway in controlling obesity. Presumably, this control has been exerted by unplanned and unorganized social forces to which the upper classes have been exposed. Ascertaining the nature of the forces specific to the control of obesity and deploying them in a rational strategy offers great hope for broad scale control of obesity. Similar or different social forces may be useful in bringing about control of obesity in other groups of the population.

Leadership in widespread efforts to control obesity is passing to nonmedical agencies, and it appears likely that this trend will accelerate; the most promising new measures for controlling obesity may lie almost entirely outside the province of the medical profession. For if obesity is indeed largely a result of the way we live, then the most effective means of controlling it may lie in altering our lifestyles. Such an undertaking as altering the habits of a nation will require changes in the powerful social and economic forces that have given rise to and that sustain them. Three institutions in our society can contribute to this effort.

- The public sector plays a vital role as a pace setter and teacher. Public pronouncements by government officials can have a strong influence upon the climate in which decisions about nutrition and exercise are made. Through regulation, financial incentives, and food services, the Government can greatly increase its impact upon obesity in America.
- The private sector, far more than the public sector, determines the lifestyles of the American people. As profit-making agencies learn that there may be profit in controlling obesity, we can expect major progress.
- Many voluntary agencies, such as the American Heart Association and the American Diabetes Association, are organized specifically to promote health. Their traditional concern, however, has been with the health of others. Promotion of the health of their own members, including control of obesity, could have a major impact upon obesity in America.

The Public Sector

Several gaps in knowledge provide important research opportunities.

- Predisposing factors for obesity are poorly understood.
- Genetic factors are clearly established for animal forms of obesity, but are less clearly identified when obesity exists in human beings.
- The role of diet in the development of obesity is poorly understood.
- Although obese people are frequently less active physically than their lean counterparts, it is often difficult to determine whether this lowered activity precedes or follows the development of obesity.
- While many individuals with obesity have an increased number of fat cells, some do not. Recent clinical studies have suggested that an increased

number of fat cells may be important in predicting the outcome of treatment. Thus, more information is needed about the factors controlling the number of adipocytes that are developed and about the factors controlling the formation and breakdown of fat within these cells.

- Behavioral factors associated with obesity have been described many times, but whether they are a consequence or a cause of obesity is poorly understood.
- Factors controlling energy balance (the relationship between food intake and the expenditure of energy in physical activity) are poorly understood. The recent development in several foreign countries of chambers in which heat loss and respiratory exchange can be measured provides a valuable tool with which to perform such studies. The use of sophisticated laboratory techniques such as gastrotomography, mass spectrometry, and the newer techniques of measuring body fat by partial immersion methods makes possible highly sophisticated quantitation of the response of the body to nutrient intake in either excess or deficient states.
- The components of food and their interaction with environmental and internal factors involved in the regulation of ingestion need to be defined in greater detail.
- Hormonal and metabolic signals and the neural substrates leading to the initiation and/or termination of eating are poorly understood.
- The metabolic and nutritional consequences of overeating may result in or accentuate a variety of metabolic diseases, including hypertension, diabetes mellitus, and gallbladder disease. Intake of excess calories as carbohydrates, fat, protein, and alcohol will burden the metabolic machinery of the body. As we understand the consequences of overeating, we may be better able to prevent it and to minimize the appearance of these chronic degenerative diseases, or treat them more rationally when they appear.
- Animal models provide valuable tools for exploring the types of obesity seen in human beings. Recent strides in defining some types of obesity may be helpful in focusing on therapeutic possibilities.

Additional models and laboratories that can breed and/or supply these animals are sorely needed.

- The many factors influencing the development of adipose tissue can be studied more effectively in animals than in humans. Unfortunately, the mechanism by which new human adipose cells develop and the metabolism of the mature human adipocyte are of prime importance in understanding the role of this tissue in the development of human obesity. Like obesity itself, adipose tissue appears to function differently in different regions of the body. These anatomic differences may be functionally important and, along with anatomic characteristics of tissue, require more accurate and complete definition. To accomplish this, more and better techniques for quantifying both the number and the size of adipocytes must be developed. While many aspects of the role of adipose cellularity in human obesity remain unknown, this area of investigation has brought to light a biologic mechanism whereby nutritional practices early in life could have a lifelong effect in predisposing individuals to obesity. These studies, along with the well-documented observation that obesity with childhood onset is the most difficult to treat, should focus attention on patterns of food intake and physical activity in childhood and adolescence.

We recommend that the Federal Government encourage and coordinate public pronouncements on health behavior, including nutrition and exercise. It is important for the Government to share with the public more information about nutrition, dietary practices, and energy balance, including information about uncertainties in these areas. We need to be candid about areas of uncertainty and controversy in existing scientific knowledge about nutrition and diet. Rapidly changing scientific evidence will undoubtedly require frequent revisions in some of the advice given to the public. We should provide more information about the range of existing views to help individuals make informed judgments about their own dietary practices in relation to their own values and their own assessment of risk.

Federal efforts should stress primary prevention of overnutrition, overweight, and obesity beginning in infancy and extending throughout life, with an emphasis in educational programs on the concept of energy balance as the chief regulator of weight.

School experiences help to set the stage for later health practices; therefore, schools should offer models for sound dietary and exercise patterns. This will require improved school feeding and food vending options, and individual exercise and fitness opportunities beyond traditional competitive team sports that reward only athletic prowess.

We commend the President's Council on Physical Fitness and urge that its activities be expanded.

We recommend:

- Extension of rules on labeling to emphasize caloric content of all packaged foods.
- Setting of standards to promote better nutrition, such as lowering the fat content in grades of meat and processed meat.
- Establishment of regulations requiring advertisements to disclose caloric content of food.
- Installation of placards encouraging the use of stairs instead of elevators and provision of facilities for walking and bicycling in communities instead of riding in automobiles.
- Offering of more options for low-calorie, more nutritious selections in government-controlled food services and government-subsidized programs, such as school lunches.
- Exploration of the feasibility of rewarding improved health behavior by means of tax rebates and lowered insurance premiums, the first to be carried out directly and the second to be encouraged by regulations.

The Private Sector

We recommend:

- That the food industry continue to develop more nutritious and lower-calorie options (decreased energy density and/or decreased portion size) in processed food and that the price of such foods not increase the cost burden to the consumer.

- That the food industry provide more information about calories and nutrients in all foods.
- That the restaurant and food service industries offer nutritional information about the foods they serve.
- That food catering services and institutions feeding their own employees provide options for low-calorie, more nutritious meals.
- That life insurance and health insurance companies expand existing public information programs and that they experiment with incentives for improved health behavior through variations in their rate structures.
- That the communications industry explore the possibility of integrating health behavior messages throughout an entire network and that nutrition and exercise receive careful consideration as topics.
- That women's magazines--a major source of information about obesity and its management--be enlisted in a more informed effort at reader education in this field.
- That health clubs, sports clubs, and sporting goods manufacturers continue and expand their promotion of exercise and that they also encourage nutrition education.
- That the medical services organized and/or sponsored by industry and labor unions also provide preventive services, and that they evaluate these efforts.

Volunteer Agencies

We recommend that the volunteer agencies continue and expand their traditional functions in the health area, including the promotion of better nutrition and exercise. We further recommend that they focus attention upon the health of their own members in addition to that of the groups they have been organized to serve.

Many of these agencies, such as the American Cancer Society and the American Heart Association, have been organized specifically to promote health. But many others serve this function as well: religious, fraternal, recreational, women's, and youth organizations. All these agencies have an excellent opportunity to improve the health of their own members in a variety of ways, including the promotion of weight control. The opportunity should be seized.

Organizations specifically aimed at controlling obesity among their members should be encouraged to collect data on their performance and to share it with responsible investigators.

The National Council on Obesity could serve as a useful coordinating agency.

1

Definitions, Criteria, and Prevalence of Obesity

Ethan A. H. Sims

Definition

The word obesity is derived from ob, over, and edere, to eat, carrying with it the centuries-old assumption that obesity is a single entity due to the single cause of overeating. Only in the last 20 years has evidence begun to accumulate which contradicts this unitary concept. Most clinical and epidemiological investigations still use obesity in its old context, as if it were a single condition caused by self-indulgence. However, the perpetuation of this assumption can distort our observations in regard to pathogenesis and risks, confound our approaches to treatment, and confuse our ability to think about priorities in research and public action. Therefore, the problems of definitions and criteria are of primary concern.

The simplest definition of obesity is a condition in which there is an excessive amount of body fat. Yet there is much to indicate that it is not always a disorder of fat storage alone. For example, obese children may have an accelerated growth of lean body mass or increases in hemoglobin, in the number of cells, or in the cytoplasmic mass of various body organs.

The definition of obesity may vary with the use to which it is put, and there are at least three definitions:

- A social definition involves clearly visible obesity, which requires no sophisticated measurements. During certain periods of history, or in geographical regions such as Polynesia, obesity may be a social asset. More generally, however, social obesity is a cause for discrimination.

- A purely statistical definition, which is useful in population studies, sees the "obese" as persons who fall in the upper 5-20 percent of whatever criterion is being used, and the "superobese" as those above the upper 5 percent. Alternatively, the superobese might be defined as those individuals who were 50-100 percent above desirable weight. Because it is easily applied, this definition is widely used and doubtless influences the social definition of obesity.

- An operational definition estimates a level of overweight based on various criteria below which there is no improvement in mortality and morbidity. This level, of course, will be different for the two sexes and may depend on race and perhaps geographical factors as well. If, as seems likely, it should be established that there are discrete subgroups of the obese and that these subgroups have quite different prognoses, any attempt to relate morbidity and mortality to a given level of obesity per se will have less meaning.

Obesity in infants and young children is also difficult to assess. When is an infant too fat? The answer may vary, as in the adult, depending on whether one uses a statistical, social, or operational definition related to health status.

In the American culture, a degree of adiposity socially acceptable in infants and young children even a century ago would be considered as too fat today. The higher prevalence of infectious diseases and the accompanying need for stored energy to withstand such frequent episodes of stress may have made the social norm of the day practical for survival and, hence, operational. A similar norm may indeed still be indicated in parts of the world where infants and young children need to contend with frequent bouts of diarrhea, enteritis, and other infectious diseases. However, in the United States and in other technologically developed countries, where the concern is primarily with cardiovascular and other chronic disease, the social norm of less adipose tissue in the young may also be operationally sound, if obesity in children does indeed predispose toward obesity in later years.

The Heterogeneity of Human Obesity

It is critical to the study of obesity to know whether the condition is heterogeneous or homogeneous. There is much to suggest that, just as there is diversity among the syndromes of obesity in small animals, so is there diversity of syndromes in humans. Studies of the body composition of obese adolescents, some of whom have had a family history of diabetes, indicate major anatomical differences. In 1959, Bjurlf first pointed out that obese patients differ in the size and the number of their adipocytes, in body build, and also in susceptibility to arteriosclerosis (13). The studies of Hirsch and his colleagues (83) and of Bjorntorp and coworkers (11) indicated that obesity of early onset is usually associated with hyperplasia and hypertrophy of adipocytes, while adult-onset obesity is usually associated with hypertrophy alone. Other reports also indicated a high correlation between age of onset and adipocyte hyperplasia, but recent more extensive studies have shown a large degree of overlap between the two anatomical types. It has been suggested that more central distribution of fat, which is typical of late-onset obesity, is more often associated with metabolic disorders. This observation was based on measurements of the relative distribution of fat and muscle in the upper and lower portions of the body. It seems unfortunate that the term android was attached to distribution of fat in the upper body and gynecoid to fat located primarily in the lower body, since sex-related factors may have no relevance. In fact, the best way to produce an "android" configuration of the body is to administer excess corticosteroids. At this stage of our knowledge, a purely descriptive terminology, such as generalized versus central obesity, might be preferable. The relationship between the accumulation of fat in the upper and central portions of the body and adipocyte hypertrophy, as opposed to hyperplasia, has been confirmed recently.

A number of other studies have borne out the concept that adult-onset obesity of central or "cushingoid" distribution carries with it a higher morbidity. A study of factory workers showed that more centrally distributed obesity correlates more strongly with hypertriglyceridemia (3). Patients with the predominantly hypertrophic form of obesity have been found to have increased susceptibility to metabolic disorders (12). There is also a difference in the pattern of fat distribution in diabetic and nondiabetic patients. A number of epidemiologic studies bear out these clinical findings. For example, in one study, an increase in weight of greater than 10 percent in men under 40 years of age correlated with subsequent development of hypertension; in another, weight gain that started in early adult life was a more sensitive indicator of subsequent cardiovascular disease than actual weight. A third study found higher incidence of both hypertension and cardiovascular renal disease in men who had been of normal weight as children but had gained weight as adults than in men whose weight had not increased (17:248-265).

A great deal of work has been directed toward finding body measurements that give the most accurate index of total body fat, but relatively little emphasis has been placed on the distribution of that fat. In fact, the most commonly used measures do not differentiate between individuals with lifelong obesity, those with obesity and metabolic derangements, and those with Cushing's disease. It may be important that the "cushingoid" patient, in whom central obesity is often associated with hypertension and non-insulin-dependent diabetes, be recognized and studied as a subtype.

Measurement of the Adipose Tissue Mass in Adults

Indexes of Overweight

There are varying degrees of complexity of estimating adipose tissue mass. Again, the methods adopted will depend on the purpose to which the data are put. All provide approximations, and few allow for estimation of the size of the lean body mass or effective muscle mass as well. One of the simplest methods is the belt test: if a belt adjusted snugly around the lower rib cage cannot be slipped down over the abdomen, the patient is certainly obese. Another is the ruler test: if a ruler placed along the sternum of a supine subject slopes upward toward the umbilicus, the subject is obese. For many situations, either visual inspection or the pinch test suffices.

There are two main methods of attempting to quantitate adiposity. One is determination of relative weight obtained when weight is expressed as a percentage or ratio to a table of desirable weight. The most commonly used guide for this is the Metropolitan Life Insurance tables based upon the data in the large Build and Blood Pressure Study of 1959. The limitations of this study have been repeatedly emphasized: the subjects were self-selected; they were classified by size of body frame, but no criterion for this was established; and they were weighed in their clothes and shoes. An alternative, based on the Metropolitan Life tables but using a single value and range, was recommended by the editorial board of the first Fogarty conference on obesity. This table of weight in relation to height for men and women, in both pounds and kilograms, provides an average weight and a range encompassing the lowest weight for "small frame" individuals and the highest weight for "large frame" individuals, as given in the Metropolitan Life tables. It is presented in table 3 of the overview.

Various indexes involving weight and height have also been tested. However, they can never provide anything more than an index of overweight, since they falsely suggest that a muscular football lineman is obese and they fail to characterize a patient with atrophic muscle mass and increased body fat. The so-called body mass index ($weight/height^2$), a weight measure divided by an area measure, has the highest correlation with independent measures of body fat; but in some series this may be as low as 0.6 or less. A nomogram for obtaining body mass index is shown in figure 2 of the overview. In children, the index produces errors in classification at the extremes of the height range. It may be hypothesized that the ratio (weight/height^2) should be considered to vary normally with age. However, the British Medical Research Council has taken the position that there is no good biological reason why such an increase should be normal; when it does occur, the rise is associated with such adverse signs as an increase in blood pressure, serum uric acid, and cholesterol. Therefore, it seems logical to refer changes in the body mass index to weight for individuals over age 18.

When increasing values are plotted for any index of overweight or obesity against parameters such as blood pressure or serum triglycerides, a generally linear relationship is obtained; there is no sharp transition to a zone that can clearly be labeled as obesity. Thus, overweight and obesity are part of a continuum, and to ascribe a sharp cutoff point may be an artificial act.

Measurements of Body Fat

Measurement of skinfolds is probably the simplest objective way to assess body fatness, but it has a greater risk of error than does measurement of height, weight, or circumference. Moreover, there is no universal agreement on the optimum number of skinfolds to measure or the best equations for calculating body fatness from skinfolds. Therefore, it is essential that more information be gained in this area before an appropriate selection can be made from among alternatives for measuring body composition. The simplest approach involves the use of a single skinfold, such as that over the midportion of the triceps muscle measured over the posterior aspect of the mid-upper arm; but considerably more reliability can be attained when additional skinfold measurements are used. Another approach involving the use of skinfolds at four sites was used in the preparation of a table for estimating percent of body fatness from the sum of the four skinfolds (table 1) (39). The skinfold sites are: mid-upper arm over the belly of biceps muscle, the triceps site mentioned above, the subscapular skinfold just below the inferior aspect of

TABLE 1.--The equivalent fat content, as a percentage of body weight, for a range of values for the sum of four skinfolds (biceps, triceps, subscapular, and suprailiac) of males and females of different ages

Skinfolds (mm)	Percentage fat							
	Males (age in years)				Females (age in years)			
	17-29	30-39	40-49	50+	16-29	30-39	40-49	50+
15	4.8				10.5			
20	8.1	12.2	12.2	12.6	14.1	17.0	19.8	21.4
25	10.5	14.2	15.0	15.6	16.8	19.4	22.2	24.0
30	12.9	16.2	17.7	18.6	19.5	21.8	24.5	26.6
35	14.7	17.7	19.6	20.8	21.5	23.7	26.4	28.5
40	16.4	19.2	21.4	22.9	23.4	25.5	28.2	30.3
45	17.7	20.4	23.0	24.7	25.0	26.9	29.6	31.9
50	19.0	21.5	24.6	26.5	26.5	28.2	31.0	33.4
55	20.1	22.5	25.9	27.9	27.8	29.4	32.1	34.6
60	21.2	23.5	27.1	29.2	29.1	30.6	33.2	35.7
65	22.2	24.3	28.2	30.4	30.2	31.6	34.1	36.7
70	23.1	25.1	29.3	31.6	31.2	32.5	35.0	37.7
75	24.0	25.9	30.3	32.7	32.2	33.4	35.9	38.7
80	24.8	26.6	31.2	33.8	33.1	34.3	36.7	39.6
85	25.5	27.2	32.1	34.8	34.0	35.1	37.5	40.4
90	26.2	27.8	33.0	35.8	34.8	35.8	38.3	41.2
95	26.9	28.4	33.7	36.6	35.6	36.5	39.0	41.9
100	27.6	29.0	34.4	37.4	36.4	37.2	39.7	42.6
105	28.2	29.6	35.1	38.2	37.1	37.9	40.4	43.3
110	28.8	30.1	35.8	39.0	37.8	38.6	41.0	43.9
115	29.4	30.6	36.4	39.7	38.4	39.1	41.5	44.5
120	30.0	31.1	37.0	40.4	39.0	39.6	42.0	45.1
125	30.5	31.5	37.6	41.1	39.6	40.1	42.5	45.7
130	31.0	31.9	38.2	41.8	40.2	40.6	43.0	46.2
135	31.5	32.3	38.7	42.4	40.8	41.1	43.5	46.7
140	32.0	32.7	39.2	43.0	41.3	41.6	44.0	47.2
145	32.5	33.1	39.7	43.6	41.8	42.1	44.5	47.7
150	32.9	33.5	40.2	44.1	42.3	42.6	45.0	48.2
155	33.3	33.9	40.7	44.6	42.8	43.1	45.4	48.7
160	33.7	34.3	41.2	45.1	43.3	43.6	45.8	49.2
165	34.1	34.6	41.6	45.6	43.7	44.0	46.2	49.6
170	34.5	34.8	42.0	46.1	44.1	44.4	46.6	50.0
175	34.9					44.8	47.0	50.4
180	35.3					45.2	47.4	50.8
185	35.6					45.6	47.8	51.2
190	35.9					45.9	48.2	51.6
195						46.2	48.5	52.0
200						46.5	48.8	52.4
205							49.1	52.7
210							49.4	53.0

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the scapula, and the abdominal skinfold just above the iliac crest at the midline. Both of these methods provide guidance in determination of obesity in children as well as in men and women. The problem of abnormal distribution of body fat is not covered in these studies, but it is anticipated that such information will ultimately prove to be of considerable value in establishing subcutaneous fat distribution patterns for various clinical conditions.

An intriguing and possibly important approach to measuring body fat is the electromagnetic technique used for determining the fat content of meat. Now this technique can be applied to living hogs, and there is some prospect that it may be applicable as a rapid, noninvasive measurement of body fat in humans. This procedure would be particularly valuable in epidemiologic surveys.

Indirect estimates of body fat can be made by laboratory procedures designed to measure the fat and fat-free compartments of the body, such as measurement of total body water by dilution of tritiated or deuterated water (^3H_2O or D_2O) and of total body potassium (^{40}K) by whole body counting. All these techniques rest on the assumption that the compartmental distribution of these elements remains a fixed quantity, an assumption difficult to support. Since the density of fat is constant, the amount in the body can be estimated by measuring the density of the entire body. However, the calculations involve assumptions regarding the density of the lean body mass, which may not be constant, mainly because of differences in skeletal mass (16).

Whole-body plethysmography may provide an improved technique for densitometry. A more direct method to determine adiposity is to inject fat-soluble indicators, such as cyclopropane or radioactive krypton, and measure their distribution in the body. These techniques provide an independent measure of body fat, but they require prolonged equilibration and have not been fully calibrated. All these methods are technically demanding, but are of value for calibrating simpler techniques used in clinical investigation. In epidemiological studies a considerable range of accuracy can be tolerated, provided the variations are random. The value of any measurement can be increased by making serial studies in the same individual.

Measurement of the Distribution of Body Fat

Perhaps the simplest of the schemes to measure the distribution of body fat was prepared to set competitive weights for schoolboy wrestlers on an objective basis. The system involves measurement of hip width, chest width, chest depth, ankle width, and height and predicts what has been termed a "minimal" effective weight. Applicability of this method to other groups has not been determined, but it has proved to be of value to others in subsequent work with young boys. A more complicated scheme for predicting lean body weight has been devised, one that may have wider application but involves more body measurements. Additional testing of the method in young men has produced generally satisfactory results.

The adipomuscular ratio was an early attempt to quantitate the distribution of body fat together with muscle. The technique involves measuring the skinfold thickness at the base of the upper and lower limbs as an estimate of fat, and the circumferences of the limbs as an index of the mass of the muscle. The ratio is determined, and a comparison is made between these values in the upper and lower half of the body. This procedure documents the larger amount of fat in the thighs of women than in the thighs of men, and also can be used to characterize the distribution of added fat in either sex. A variety of body measurements have been taken, with the aim of finding those that may form the basis of the best estimate of total body fat. In a study of the incidence of hypertriglyceridemia in factory workers, the ulnar skinfold thickness was used as an index of longstanding generalized obesity, and the subscapular skinfold as an index of weight gain in adult life (3). In subjects with small ulnar skinfolds, i.e., those not previously obese, a positive correlation was found between the subscapular skinfolds and the elevation of triglycerides. The triceps skinfold was intermediate between the other two in reflecting recent and central, as opposed to generalized and longstanding, weight gain.

Although most recent epidemiologic surveys have available, at best, measurements of the subscapular and triceps skinfolds, these data provide some opportunity to test the relative importance of central, as opposed to generalized, deposition of fat in relation to morbidity. It is difficult at this point to determine exactly which body measurements would provide an optimal measurement of the distribution of body fat, since so little attention has been given to this question and adequate studies have not been done. In preparing this report to evaluate whether it is indeed important to consider subtypes of obesity with respect to distribution and age of fat deposition, we have analyzed the data from the Health and Nutrition Examination Survey (1971-74) (HANES I). This large survey has provided geographically representative data from 6,000 black and white men and women ages 29-65.[1] Since both subscapular and triceps skinfold measurements were made, it was possible to test the hypothesis that central obesity is more closely correlated with diabetes, hypertension, and hypercholesterolemia than is peripheral obesity. Conclusions from the analysis are as follows:

- Subscapular and triceps skinfold measurements were highly related in a linear fashion.

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[1] We are indebted to Dr. Michael Hatwick and to Mr. Sidney Abraham of the National Center for Health Statistics for making the data available in advance of the final analysis. Selected data processing and statistical analysis were carried out by Dr. Jean-Pierre Habicht, a member of this task force and a former member of the National Center; by Ms. Dorothy Blair in Dr. Ellsworth Buskirk's laboratory at Pennsylvania State University; and by Dr. David Sylwester of the Biometry Facility of the University of Vermont.

- For the four groups, divided by race and sex, there was a curvilinear relationship between subscapular skinfolds and age, with the lowest values at the lowest and highest ages. The peak values were reached in black men ages 30-40, in white men ages 30-59, in black women ages 50-59, and in white women ages 50-65. For the triceps, the curves were similar, with a tendency toward earlier peaking, except in the case of black men.
- The relationship of the various parameters to systolic blood pressure was extensively examined. It was found that the linear relationship to predict systolic blood pressure from subscapular skinfold values had the same slope for each age and sex group. It was therefore possible to subtract from each subject's systolic value the contribution predicted by that subject's subscapular value, thus obtaining the systolic value residualized on subscapular values. The appropriate formula was

$$\text{RSYST} = \text{Systolic } (0.63498)(\text{subscapular skinfold}).$$

Regression analysis showed that the triceps skinfold measurement gave no added predictive value.

- Since age was found to have significant predictive value, but with different slopes for each race and sex group, it was possible to start over and residualize the systolic values on age, using different slope coefficients for each race and sex group. It was then possible to carry out regression analysis of the systolic pressure residualized on age and to assess the effect of sex, race, triceps skinfold, and subscapular skinfold. There were significant effects due to the following:

	Coefficient	S.D.	F	p-value
sex	-18.5	0.58	1014	0.001
race	4.9	1.23	15.8	0.01
race x sex	-12.0	1.48	66.0	0.001
subscapular	0.57	0.02	476.0	0.001
triceps		-	2.08	>0.05(N.S.)[a]

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[a] Not significant.

The values for the interaction of race and sex (race x sex) indicate that the difference between black men and white men was not the same as that between black women and white women.

The above analysis of systolic blood pressure residualized with respect to age explained only a quarter of the variance ($R^2 = 23.9$). This is a high value under the circumstances. However, it remains an epidemiological challenge to increase this. A host of other variables, such as social and economic factors, smoking habits, and use of oral contraceptives, may be of importance.

The fact that there was no predictive value of the triceps skinfold for blood pressure, whereas the subscapular skinfold was correlated with blood pressure, was consistent with the hypothesis that persons with more central deposition of fat are more prone to hypertension. A similar relationship held for the prevalence of diabetes and for the incidence of hypercholesterolemia defined as a value of total serum cholesterol greater than 250 milligrams per 100 milliliters. Serum triglyceride measurements were not included in the survey; hence the relationship of this variable to central obesity could not be directly tested. The data, however, seem to suggest that subtypes of obesity must be considered in evaluating the relationship of the types of obesity to risk factors for heart disease. Future studies should include ulnar skinfolds and other measures of the distribution of fat.

Classification of the Obese

Various attempts over the years to classify obesity were reviewed in the summary volume of the first Fogarty conference on obesity, and a data base classification based on that developed at the University of Vermont was suggested (19).

It has been standard clinical practice to use the designation exogenous obesity once gross endocrine disorder and brain damage have been eliminated. Since all obesity is exogenous with respect to energy balance, this pseudodiagnosis merely serves to deaden further thought. In addition, the designation exogenous has come to imply that the patient is at fault for allowing such a state to develop, and this in turn relieves the physician of the need to pursue prime causes and possible points of attack.

Many factors, such as family lifestyle, inactivity, psychological disturbances, occupational problems, and predisposing medications, may contribute to development of acquired obesity.

Even when obesity appears in successive generations of humans, it may not reflect genetic factors. Environmental patterns associated with family life may be even more important, although a combination of the two is most likely. There is impressive evidence, based on studies of mono- and dizygotic twins, that the influence of inheritance may be a strong or, indeed, overpowering factor in the development of obesity. This is certainly the case in several varieties of obesity followed by overt diabetes in small animals (25). The combination in humans might well be called "diabesity." Hypertension may be similarly related. On the other hand, in very extensive recent studies of children adopted at an early age, of siblings, of husbands and wives, and of overweight persons and their pets, it has been suggested that, although fatness does follow family lines, it is learned, not inherited. The explanation for this may well be that certain subtypes of obesity are genetically transmitted, while other subtypes are behavioral. Until this confused situation is clarified, we suggest that patients not be assigned to a classification of genetic or familial obesity.

In any evaluation of individuals with obesity it is helpful to obtain a full data base. The extent and nature of this will vary with the goals of the evaluation. For an epidemiologic study, the questions posed before the study is designed will determine the data base. Obesity has shared with diabetes the problem of inadequate definition. The report for the Workgroup on Epidemiology of the National Commission on Diabetes points out that important correlations in clinical investigations may be lost: "In part, because the purposes of questions related to each type of diabetes have not been formulated with health statisticians, national data which differentiate between these types of obesity are not available" (117).

The problem-oriented approach to developing a data base is well adapted to clinical management of obesity. A defined list of problems serves as a basis for defining goals and formulating plans; it enables each person caring for a single aspect of a patient's illness to coordinate his or her efforts with others, and it subsequently provides a basis for audit as to how well the plans have been carried out.

Recently, an attempt was made to develop an algorithm for evaluating patients with obesity (22). Such an approach can properly be expanded and adapted to computer processing, both for obesity and for related metabolic disorders.

Limitations and Relevant Problem List for the Types of Obesity

At the time of the first Fogarty conference on obesity (19), it seemed reasonable to provide an anatomical classification of obesity into 1) patients with hyperplasia and hypertrophy of adipocytes, usually of early onset; and 2) those predominantly with hypertrophy of adipocytes. However, in a review of an extended series of patients, a considerable overlap in types was found, suggesting that late-onset obesity may be associated with cellular hyperplasia and vice versa (83). A more complete data base for subjects selected for such studies may clarify this confused area. On the other hand, further work may show that there is a continuum with respect to cellular hyperplasia. Less technically demanding procedures are needed for sizing adipocytes and estimating total body fat. For clinical investigation, the anatomical status of the patients should be established; we suggest that it is permissible to classify a patient anatomically for clinical purposes as "early onset, universal distribution of obesity with probable hyperplasia of adipocytes," or "adult onset with central distribution."

Assigning an etiologic diagnosis may be equally difficult. Certain relatively rare conditions associated with obesity can be diagnosed with assurance. But in the majority of patients, no such evidence is at hand (16). Relegating these persons to a diagnostic category such as "obesity, etiology undetermined" contributes neither to general understanding nor to patient welfare.

Prevalence

An epidemic of obesity, and of the non-insulin-dependent diabetes and hypertension strongly associated with obesity, continues in most population groups in this country. The prevalence of obesity was reviewed at the time of the first Fogarty conference on obesity and is summarized in tables 1 and 2 and figure 1 of the overview.

According to the Seven Country Study, Americans have tied with Italians for the greatest prevalence of men 10 percent or more over standard weight and have double the prevalence of obesity, as defined by a sum of subscapular and triceps skinfold thickness greater than 29 millimeters (95). Successive groups of military inductees in the United States are increasingly both heavier and taller, and each cohort of men in the prospective Framingham Study is heavier at corresponding ages than its predecessor (chapter 6). The latter study, however, has shown that for women the contrary is true; those born later in the century are correspondingly lighter than their predecessors, despite an increase in height. This probably reflects the pressure of changing fashions, as well as a lifestyle which may include greater physical activity.

The incidence of obesity as measured by skinfold thickness differs considerably among ethnic groups. The Ten State Nutrition Survey of 1968-70 showed that obesity was more common among white than among black men, but the opposite was true for women (79). The level of income did not affect the incidence of obesity in adolescents; but for both black and white men, lower income levels were associated with a lower level of obesity. In younger women, obesity was more prevalent in the lower socioeconomic groups. In older women, both black and white, lower income was associated with a lower prevalence of obesity. Data from the HANES I survey indicate that subscapular skinfolds were strikingly greater in black women than in white, although men did not differ significantly between the races (figure 1, overview).

Information on the prevalence of obesity in other countries was reviewed by Christakis (34) and by the publication Research on Obesity (88). Investigators concerned with the epidemiology and impact of obesity find themselves working under much the same handicap as that noted in the recent report of the Workgroup in Epidemiology of the National Diabetes Commission: "Persons with insulin-dependent diabetes and those with insulin-independent diabetes have different natural histories. Yet, in part because the purposes of questions related to each type of diabetes have not been formulated with health statisticians, national data which differentiate between these types of diabetes are not available" (117). Exactly the same may be said about the various types of obesity, except that the differentials are not as sharp as those between the two main types of diabetes. Information regarding the interrelationship of obesity and diabetes is also inadequate. When the National Institutes of Health Task Force for Hypertension reviewed the relationship of hypertension to obesity, the same inadequacy of data became apparent (87:1623-1631). Since hypertension associated with obesity is responsive to aggressive dietary treatment (126) and increased physical activity, this is a matter of national importance.

Epidemiologic studies of obesity that have included socioeconomic status indicate that social and economic factors are strong determinants of obesity. As Garn has stated (56), "When we involve measures of socioeconomic status, we find further problems with a simple genetic explanation. For poor boys and poor girls are leaner than those more affluent, and this statement may be generalized to...poor men as well. But in adulthood, it is the poor woman who is fatter and the rich woman who is leaner, and fatness decreases linearly with increasing income in women....If the level of fatness follows socioeconomic status or educational level in such a circuitous way, then it is difficult to credit a purely genetic explanation. At the present time, obese women in the United States outbreed lean women nearly 2:1. Since this indicates that our now-fat country is on its way to becoming fatter, we need to find out why."

As noted above, it appears that hyperplasia of adipocytes may not be as strong a determinant of adult-onset obesity as was once thought, and that additional adipocytes may be recruited in adult life under pressure of marked weight gain. This, together with the epidemiological data, is encouraging since it suggests that by modifying social, economic, and familial behavioral patterns the epidemic of obesity may be lessened.

2

Pathogenesis of Obesity: Energy Intake and Expenditure

Judith Rodin

Energy Intake

Central Factors

Ventromedial Hypothalamic and Lateral Hypothalamic Regions

Background. Until recently it was widely held that food intake and body weight were controlled and regulated by two centers or systems in the hypothalamus. According to this view, feeding was initiated by a lateral hypothalamic (LH) "feeding center," whose activity reflected the energy state of the organism, and was terminated by the inhibitory action of a ventromedial hypothalamic (VMH) "satiety center" on the LH center. VMH activity, in turn, was modulated by postingestive satiety signals. In addition to controlling food intake, the VMH and LH centers appeared critical in the long-term regulation of body weight and were thought to contain a setpoint(s) for body weight, that is, an ideal level.[1] Extrahypothalamic feeding mechanisms were known to exist, but they did not seem as important as the dual hypothalamic centers and, in fact, were thought to influence food intake via their effects on the hypothalamus. The dual center model has served us well, but is now untenable in light of recent research. Unfortunately, an alternative model of the central control of food intake is not available to take its place, and this presents a major unresolved problem.

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[1] Against which the current body weight of the animal is compared.

LH feeding syndrome. Identification of the LH as a feeding center was due to the discovery of the aphagia syndrome produced by LH destruction. It is now known that this syndrome is largely, but not completely, the result of damage to the dopaminergic nigrostriatal pathway. Much research interest has therefore focused on this pathway, and the LH has, in a sense, fallen from grace. Nigrostriatal damage, however, produces widespread behavioral deficits which are not limited to the control of food intake. It therefore appears that this pathway is not part of a feeding system per se, but may subserve some more general function, such as the integration of sensorimotor information.

Although LH neurons are not responsible for the aphagia syndrome, at least some of them are involved in food intake regulation. This is indicated by the feeding effects produced by small LH lesions that spare the nigrostriatal pathway, by the feeding effects of synaptically active drugs injected into the LH, and by the electrophysiological recordings from this area. Research should continue on the specific feeding functions of the LH, as well as on the pathways that course through it.

VMH feeding syndrome. The hyperphagia and obesity produced by VMH destruction (known as the VMH syndrome) have been extensively studied, and our understanding of this syndrome is being drastically revised in light of new data. Hypothalamic hyperphagia has long been associated with the ventromedial nucleus, but it now appears that this nucleus is not directly involved in the syndrome. Rather, current evidence indicates that hyperphagia and obesity result from damage to a longitudinally situated pathway that passes by the VMH. Where the pathway originates and terminates, and its relationship to recently discovered monoamine pathways is the subject of ongoing research. In particular, the anterior hypothalamus and paraventricular nucleus of the hypothalamus have been implicated as being critical loci.

The functional disorder responsible for the hypothalamic obesity syndrome is also an unresolved issue. Historically, two theories have been emphasized: the short-term satiety theory and the lipostatic theory. The short-term theory holds that VMH-damaged animals overeat because they are insensitive to the satiating effect of recently ingested food, whereas the lipostatic theory holds that VMH animals are insensitive to the feeding inhibitory effect of excessive body fat stores. Although the VMH is frequently referred to as the "satiety center," there is little evidence that VMH damage impairs postprandial satiety mechanisms. The satiety hypothesis was based primarily on indirect or negative evidence, and there is little reason to believe that hypothalamic obesity results from a short-term satiety deficit. The lipostatic theory is more difficult to evaluate since little is known about the mechanism by which body fat is regulated. Simple setpoint models of hypothalamic obesity no longer seem tenable, given the complexity of the behavioral changes induced by VMH damage. Furthermore, it is now apparent that body weight may not be actively governed by feedback signals from adipose tissue but may be passively governed as the result of the regulation of other nutrient stores.

Current theories of hypothalamic obesity focus on the metabolic and motivational correlates of the VMH syndrome. There is considerable evidence that VMH damage alters hormonal and metabolic functions, but whether these changes are causes or consequences of the obesity remains to be resolved. Most emphasis has been placed on the increased insulin levels of the VMH-damaged animal. That hyperinsulinemia may be a causal factor in hypothalamic obesity is suggested by several findings: for example, hyperinsulinemia may precede the development of hyperphagia and obesity, and its degree has been correlated with subsequent weight gain; furthermore, preventing hyperinsulinemia by vagotomy, beta cell destruction, or pancreas transplants attenuates or eliminates hypothalamic obesity. While these results demonstrate the critical role of insulin secretion to the obesity syndrome, they do not necessarily mean that the sole, or even the primary, effect of VMH damage is to increase insulin release. Further research is needed to integrate the central and peripheral effects of VMH damage as they affect feeding behavior.

The motivational state of the VMH-damaged hyperphagic animal has been reevaluated in light of recent behavioral findings. Rather than decreasing hunger drive, VMH damage enhances food motivation; but it does so in a way that is not fully understood, as indicated by the variety of different hypotheses presented. That is, the food-motivated performance of VMH-damaged animals is greatly influenced by such variables as the type of feeding schedule used, the level of food deprivation, the pretraining variables, and the nature of the reward. Part of the problem is that current understanding of hunger motivation is inadequate, and new behavioral models of food motivation need to be developed. These models must incorporate not only homeostatic variables but also nonhomeostatic factors, including hedonic as well as environmental variables. The VMH syndrome, in fact, may be more helpful to our understanding of motivational systems than vice versa.

The phenomenon of VMH-lesion-induced hyperphagia has given rise to a plethora of studies on 1) the behavioral changes (e.g., finickiness, exaggerated reactivity to nongustatory stimuli) of VMH-damaged rats, 2) the capability of such animals to regulate their caloric intake, 3) the metabolic changes in VMH-lesioned rats, and 4) the neural connectivity of the VMH with the brain areas thought to be involved in feeding. To the extent that the VMH syndrome is a window to the neural control of appetite, this concentration of research is appropriate. Unfortunately, there is little agreement on what all the work means. Is the ventromedial hypothalamus a satiety center controlling short- or long-term regulation of food intake? Does the ventromedial hypothalamus sense nutrient availability in the circulation directly, or does it get its information only indirectly from the sensors located outside the brain? Does the enhanced feeding of VMH-damaged animals reflect a direct neural control of appetite, or do the lesion-induced peripheral metabolic/endocrine changes themselves stimulate appetite? If it is the latter, how can one account for the other behavioral changes of these animals, particularly their enhanced reactivity? What neural tissue is responsible for the feeding effects--if not the ventromedial nucleus itself, then what?

For each of these questions, evidence exists suggesting one or another hypothesis.

Neuroendocrine Links--Noradrenergic and Serotonergic Pathways

Feeding in relation to brain norepinephrine and serotonin. Norepinephrine's (NE) role in food intake has been recognized since Grossman found that administration of this substance to hypothalamic sites elicited feeding (74). Recent advances in this field include: 1) the fact that the locus for NE's action appears to be centered in the medial anterior hypothalamus or paraventricular nucleus, and 2) the finding that food intake in cats can occur following the release of endogenous brain stores of NE.

Recent complexities, however, have been introduced by the finding that overeating can follow destruction of the ventral NE-containing bundle. The paradox that both excesses and deficiencies of NE transmission can lead to enhanced food intake has been a formidable obstacle in our understanding of the role of NE in eating behavior. A possible resolution comes from findings which suggest that there are two independent NE-sensitive receptor sites in the hypothalamus that are involved in food intake, such that stimulation of one leads to eating, while stimulation of the other suppresses it. The implication is that NE-induced eating depends upon stimulation of the former sites, while overeating may be induced by a denervation of the latter sites. The latter concept has been supported by findings in rats.

A final important area of investigation concerns the measurement of hypothalamic NE during feeding. For example, it has been reported that rats have a higher content and higher turnover rate of NE within the perifornical and dorsomedial hypothalamic areas at times of the day when the feeding rate is high. The studies used a push-pull cannula system to measure the release of NE from the dorsomedial, perifornical, and anterolateral hypothalamus of freely moving rats. During feeding, NE release from dorsomedial and perifornical areas was significantly elevated.

The possibility that brain serotonin (5-HT) is involved in food intake has received experimental support in the last 3 years. Central administration of parachlorophenylalanine, which depletes brain 5-HT, produces overeating and weight gain. More permanent destruction of 5-HT-containing neurons, using 5,7-dihydroxytryptamine, results in enhanced growth and elevated food intake in young rats. Whether the elevated food intake is primary or secondary to prolonged growth, however, remains uncertain. Paradoxically, the destruction of brain 5-HT-containing neurons has been found to attenuate the hyperphagia resulting from VMH lesions. Finally, there has been evidence that fenfluramine may have its anorexic effect via a release of brain 5-HT.

Central Receptors

Much research has been devoted to establishing the existence of central receptors in the control of food intake and body weight. The most extensive evidence exists for glucoreceptors or glucosensitive neurons in the VMH and LH. VMH and LH neurons, for example, alter their firing rate as blood sugar levels change, even in decerebrate preparations. Hypothalamic neurons also respond to the direct electro-osmotic application of glucose, and the response rate may be altered by the simultaneous application of insulin. There is also some evidence to suggest that hypothalamic neurons are sensitive to free fatty acids, amino acids, and cholecystokinin, but much further research is needed to establish that central receptors exist for these substances. Little attention has been devoted to establishing the criteria needed to demonstrate the existence of central receptors, or to attempts to test these criteria systematically. Minimally, the proposed receptor must: 1) selectively respond to changes in blood level of the putative stimulus; 2) selectively respond to direct application of physiological amounts of the putative stimulus; 3) alter food intake when stimulated with the putative substance; 4) when destroyed, prevent the normal feeding response to the putative stimulus. In the case of the proposed hypothalamic glucoreceptors, there are electrophysiological data to satisfy criteria 1 and 2, but few behavioral data to satisfy criteria 3 and 4. In contrast, studies of proposed hypothalamic osmoreceptors for thirst have been more successful in meeting all four criteria.

In addition to possibly containing its own receptors, the hypothalamus clearly receives input from peripheral receptors, including both visceral (gastric, intestinal, hepatic) and somatic (olfactory, gustatory, visual), and may be an important convergence site for these two systems. For example, unit activity in the LH is modified by hepatic-portal infusions of glucose, with both the splanchnic and vagus nerves being implicated. LH neurons also are activated by visual stimuli associated with food, but not nonfood objects; and the neural response is influenced by the state of hunger and satiety. The same units that respond to visual or gustatory food-related stimuli are activated by brain stimulation reward, which has suggested that such brain stimulation may be rewarding because it mimics the sensory effect of food. Related to this are the findings that gustatory stimulation can modify the LH self-stimulation rates and stimulus-bound eating produced by LH stimulation. In line with these results, damage to the hypothalamus interferes with the feeding responses to ingested or infused glucose as well as producing a failure in sensory responses.

Peripheral Factors

Background

As yet there is no clear understanding of the peripheral control of food intake, although there are several possible neural signals that could inhibit it: stretch receptors have been found in the stomach wall that send neural impulses to the brain through the vagus nerve; there are receptors sensitive to the acidity of the gastric contents; and receptors in the wall of the small intestine respond to the presence of glucose or amino acids in the lumen. Afferent impulses from the gastrointestinal tract have not been thoroughly investigated; some researchers have recorded from the vagus nerve, while others have recorded from the intestinal nerves that could have been either sympathetic or parasympathetic. Fully 90 percent of the vagus nerve is afferent, and 50 percent of the sympathetic system is afferent.

Neural Regulation

A few studies have shown that nerves are not essential for regulating food intake. There are no studies in which a complete nerve section has been done on an animal in a single operation; such operations are usually fatal, for reasons that are not clearly understood. Nerve sections usually make the animal unwilling to eat and do not lead to gross overeating. A few studies have done stepwise denervations by cutting the vagus and left and right sympathetics in separate operations spaced over a number of months. With several operations, the animals recover and appear to eat normally, despite the absence of neural connections between gut and brain. Grossman et al. demonstrated that denervated dogs eat normally, and they also respond to insulin injections by increasing their food intake, showing that insulin injections do not depend upon neurally mediated peripheral actions such as gastric acid secretion to stimulate food intake (73). Harris et al. confirmed the observation that denervated dogs eat normally and showed that amphetamines reduce food intake in normal and denervated dogs (77). Unfortunately, neither study checked for completeness of the nerve section, and it remains possible that some nerves were missed or that regeneration of severed nerves led to reestablishment of some neural control. The last possibility is particularly relevant since the stepwise denervations usually took several months to complete. Nevertheless, it must be true that feeding behavior can remain normal after neural connections between the brain and the gut have been substantially reduced. While this observation means that it is unlikely that a strictly neural mechanism controls food intake, it does not argue that nerves are not involved in the regulation of feeding behavior in the intact animal. The nerves modulate secretion, motility, and blood flow, all of which may play some role in the regulation of feeding behavior.

Humoral Regulation

The other possible communication route is through the bloodstream. Several authors have theorized that one or another nutrient is involved in controlling feeding behavior. The most prominent theory is that food intake is controlled by the presence or absence of an arteriovenous difference in blood sugar level. The hypothesis has had some support based on correlations, but in several studies glucose has been injected directly into the bloodstream with little effect on feeding behavior. Furthermore, meat is effectively satiating even though it consists mostly of fat and protein. Other theorists have proposed that absorbed amino acids or the amount of body fat controls food intake. The latter theory does not specify the way in which body fat is monitored, but it is possible that the brain senses the level of free fatty acid in the blood.

The importance of absorbed nutrient for the short-term regulation of food intake is minimal, according to the results of studies with crossed-intestines rats. In these studies, food eaten by one rat enters its stomach and travels through some of its duodenum before crossing into the intestine of the other rat. Approximately equal amounts of glucose and amino acids are absorbed into the bloodstreams of both rats. The fed rat is fully satiated, and the unfed rat remains hungry despite the nearly equal absorption of food into the two rats. Food intake does not appear to be controlled by the amount of absorbed nutrient.

Hormonal Regulation

The third possibility is that a hormone controls food intake. It has been argued that increased levels of the intestinal hormone cholecystokinin reduce food intake (136). Certainly, a sufficiently high dose of cholecystokinin diminishes feeding behavior, but the effect may be pharmacologic rather than physiologic. Two earlier studies found no evidence for a physiologic effect of cholecystokinin on food intake (61,100). The results from rats with crossed intestines also suggest that cholecystokinin does not regulate food intake.

The actual internal signal that produces satiety remains obscure. It could be some other gastrointestinal hormone or several others. It could also be a combination of neural, humoral, and hormonal signals, each relatively ineffective by itself. Psychological factors such as conditioned satiety, stress, and external cues will play a role in determining the amount of food eaten.

Influence of the Liver

A number of authors have argued that the liver might produce a signal that provokes satiety. Recordings from the vagus nerve show that there are hepatic glucoreceptors that decrease their firing rate when glucose is injected into the portal vein. It has been argued that these hepatic glucoreceptors control food intake, which is particularly noteworthy in light of findings showing that electrical blockade of the vagus nerve leads to a decrease in food intake. Glucose infusions into the portal vein have been shown to diminish food intake effectively in 24-hour food-deprived rabbits, but they had no effect on freely feeding rabbits (119). In addition, the portal infusion of 2-deoxy-d-glucose (2-DG) could elicit eating in normal but not in vagotomized rabbits. The latter observation suggests that the 2-DG-induced feeding is initiated in the liver and conducted through the vagus nerve.

A number of researchers have concluded that the liver can affect food intake when special nutrients are infused into the blood. Fructose, a sugar utilized by the liver but not by the brain, has been shown to counteract the feeding response induced by insulin infusion. It is believed that the liver might be involved in preventing this insulin-induced feeding behavior, but it has also been pointed out that the ketone β–hydroxybutyrate, which is metabolized in the brain but not in the liver, is also effective in reducing insulin-induced feeding.

These experiments have shown that the liver can affect feeding behavior, particularly in unusual situations where glucose utilization has been manipulated. It is not very likely that the liver controls food intake under normal conditions. The studies with crossed intestines in rats show considerable absorption of food from the intestines of the rat that was not fed. This absorbed food, including glucose, must pass through the liver before entering the general circulation and, therefore, would be expected to alter its metabolic state. The absorbed food does not change the rats' feeding behavior. Furthermore, several studies have shown that rats with portacaval shunts eat normally and show minor weight loss. The absorbed food eaten by these rats goes directly into the general circulation and reaches the liver only through arterial blood. Much of this food does not pass through the liver since it is taken up by the body tissues before reaching the hepatic artery. In short, if the liver controlled food intake, rats with portacaval shunts should increase their food intake, which is contrary to the observed results. Finally, several studies have shown that animals can survive with a transplanted and thus totally denervated liver.

An intact hepatic branch of the vagus nerve may be important in feeding behavior induced by intravenous injection of 2-deoxy-d-glucose or insulin, but it is not essential to the normal regulation of feeding behavior.

Dietary Factors

Although most research has focused on physiological and genetic factors in obesity, it is clear that environmental conditions, particularly those related to the diet, can influence food intake and body weight. For example, obesity can be readily induced in otherwise normal laboratory animals by offering them high fat diets, sugar solutions in addition to lab chow, or a variety of palatable snack foods. Such diet conditions, furthermore, can greatly potentiate the obesity produced by specific disorders, as in the cases of hypothalamic, ovarian, or genetic obesity in the rat. Preweaning overnutrition may be of particular importance since it may increase adipose cell number as well as size and, therefore, produce permanent effects on body weight and fat content. These findings are important because they indicate that obesity need not always be the result of some specific neural, hormonal, or genetic disorder and because they indicate that body weight regulation is less precise in laboratory animals than is commonly believed, based on studies using lab chow diets.

The Vagus

The vagal nerve seems to occupy a key position among factors regulating food intake. While VMH lesions in rats lead to obesity, this may be prevented by transecting the vagal nerve. Furthermore, insulin secretion can be increased via the vagal nerve. Recently, it was shown that immediately (10 minutes) after VMH lesions, insulin levels increased in response to an intravenous glucose injection. Whether this is associated with the vagal nerve is not known as yet, but it may well be. In any case, it seems that the VMH exerts a direct inhibitory control on insulin secretion and may in this way influence caloric intake. Whether this is true in humans is presently unknown. However, hyperinsulinemia prevails in obesity, and this may influence factors possibly regulating food intake (glucose, amino acids, free fatty acids), as discussed above, as well as peripheral metabolism. In this context, recent findings seem relevant showing that the cephalic phase of insulin release (induced by showing the animal food for a short time), which presumably is mediated by the vagal nerve, is increased in obese individuals. Whether this is primary or secondary to obesity is not known, but the latter seems more likely. However, it may well influence food intake and thus contribute to the maintenance of the obese state. The effect of anticholinergic agents on insulin release as well as on food intake should clearly be evaluated.

Environmental and Social Factors

Nonphysiologic considerations play a dramatic role in energy intake and expenditure. Our attitudes toward thinness and beauty, which are culturally determined and socially reinforced, may be among the most important factors involved in regulating body weight. While the role of these conscious controls is major, intentional self-regulation is terribly fragile. As Herman's work shows, those individuals who by self-report appear to exercise the most conscious dietary restraint seem to be those who also lose this control most readily under conditions of externally imposed overeating, distraction, emotionality, and alcohol consumption (82). Thus, long-term regulation by conscious control can be easily disrupted by manipulations that induce overeating.

In the short term, situational-environmental food cues including the type and number of food choices (especially palatability), food habits and practices, and beliefs about the caloric value of food all dramatically influence the amount consumed. We are struck by report after report of how poorly persons of all weights regulate their food intake in response to covert changes in the caloric value of the food. The evidence shows clearly that self-report of hunger almost never picks up these manipulations, and people may not really be able to perceive caloric variations without the benefit of information from cognitive and external cues. While experimentally we can separate cognitive and visual cues about caloric density from actual caloric value, in the real world they do correlate. Therefore, through conditioning, cognitive and visual cues have come to play an important role, imparting information that is accessible to the individual. We need studies to determine how energy balance might proceed over a long period of time without these cues.

The opposite strategy has also been used successfully in several studies. When individuals are placed in nonlaboratory settings where external food cues are abundant, where the cuisine is novel, where eating is virtually ad libitum, many gain weight. The increase is correlated with the extent to which these people, by independent assessment, are responsive to external and sensory food cues. However, after several weeks the weight gain ceases in most of these subjects. Whether the "stop" mechanism is psychologic, physiologic, or both, we do not yet know.

External cues may also influence consumption because of their activating component. They may arouse the organism, in addition to motivating and directing it. Here a neuroendocrine link may be implicated through monoamine pathways. Moreover, arousing the organism through other means may raise the incentive value of the food cues.

Finally, external food cues may be especially important because of their association with the postabsorptive consequences of eating and the general energy state of the organism. This would make them high in informational value.

We can ask whether greater responsiveness to external cues, which is relatively common among the moderately obese and can dispose to weight gain, is genetically determined or is generated by the effects of early feeding experience on energy needs. The inability of the subject to predict the physiological consequences of external influences, such as time, food stimuli, and perhaps emotional stimuli, would likely interfere with the ability to discriminate and with internal control of appetite. This deficiency leads to internal controls and relatively strong responsiveness to the physical intensity of a stimulus, rather than to its eventual effects. While hunger, satiety, and individual tastes must be learned, cognitive control of feeding should not be opposed to physiological control. When individuals treat disguised nutrients such as diet soda erroneously, they are, at least in part, transferring well-conditioned responses into survival instincts. Time of day, expectation of food, beliefs about past intake, and social feeding tendencies are not only cognitive and social cues, they are cognitive and social cues that can be used to predict physiological consequences in the individual. The design of foods and the scheduling of meals in daily life are integrated into biopsychological variables in the individual. In most cases, information at physiological, cognitive, and environmental levels will probably be necessary to predict obesity.

Long-Term Controls

Studies now appearing suggest that fat cell size may be regulated, although the mechanism involved and the nature of this regulation are not yet clear. Nevertheless, some possibilities exist for future investigation. Large fat cells seem to respond to lipolytic stimuli; in fact, in vitro lipolysis increases as a function of fat cell size, and no dose-related resistance has been found in large human fat cells. Furthermore, raised free fatty acid levels usually accompany obesity. If fat cells provide a "feedback" regulator directly, it may be either glycerol or free fatty acid. Glycerol cannot be utilized by the fat cells again and is released into the bloodstream, taken up by the liver, and used as a gluconeogenic substrate. Recent evidence indicates that glycerol can influence dietary intake (156). The possibility exists that gluconeogenesis from glycerol in the liver can in some way be transmitted to the brain as an index of fat cell metabolism. In this context, it is of interest that vagal activity may be influenced by the glucose concentration in the portal blood. From a quantitative point of view, glycerol is probably not a sufficiently important gluconeogenic substrate to exert a feedback regulation in this way. However, glycerol concentration may in a similar way exert an influence over satiety, although nothing is known about this to date.

The other possibility is that the free fatty acid levels or free fatty acid metabolism may regulate dietary intake and/or metabolic efficiency (see below). Undoubtedly, several hormones that raise the free fatty acid levels, such as catecholamines and glucagon, reduce food intake. Conversely, insulin lowers free fatty acid levels and raises food intake. However, free fatty acid changes parallel glucose changes, and these may well influence dietary intake via the well-known "glucostatic" theory of food intake, which hypothesizes that satiety occurs when glucose utilization increases and that hunger reflects lowered rates of glucose metabolism.

Although free fatty acid level or free fatty acid metabolism appears to be a likely regulator of body weight, the lability of plasma levels argues against it. However, since caloric intake may be rather poorly correlated to the daily energy expenditure, long-term regulation in which excessive caloric intake can be dispensed through heat production, for instance, should be evaluated. Under these conditions, free fatty acid metabolism may well be of importance.

Energy Expenditure

Background

It has been asked whether the efficiency with which individuals use energy remains constant at all times and under all dietary conditions. Ever since Lavoisier demonstrated animal respiration, there has been the tendency to assume that animals constantly burn their substrates with the same efficiency. There is now evidence for the existence in humans and "lower" animals of a diet-induced adaptation in metabolism during both over- and undernutrition that is responsible for changes in thermogenesis and, therefore, in the efficiency with which nutrients are used. Clinical situations have also shown large discrepancies between the amount of energy predicted as necessary to maintain energy balance and the amount actually needed. This point is illustrated by the patient with a malignancy which seems too small to account for the disposal of the extra calories necessary to maintain equilibrium, and by the postsurgical patient who requires more calories than expected to maintain energy balance and to begin recovery. These situations are complicated, but there is no evidence to disprove the theory that they represent altered states of metabolism that waste administered energy. During starvation, mechanisms appear early as adaptive responses to the lack of fuel, so the body draws upon its own stores of energy. At the same time, alterations occur in the utilization and expenditure of calories, allowing essential life functions to be maintained for periods longer than otherwise expected. Alteration in the rates of synthesis and renewal of cellular components is part of this adaptation. On the other side of the scale, there is now evidence that overnutrition may be associated with differences in the efficiency of weight gain and in the relative number of calories necessary to maintain added weight.

The Role of Exercise

Normal adults differ substantially in energy expenditure. Even when matched for age, sex, and weight (especially the weight of lean tissue), individuals may still differ by 30 percent.

It has been concluded, based on a review of current data, that physical exercise is not the main factor determining energy expenditure or intake in affluent societies (58). It is unrealistic to expect people to increase their energy expenditure by more than about 360 Cal (1.5 megajoules) daily, although doing so may have considerable psychological and physical benefits.

While simple caloric expenditure by exercise may not be critical, recent evidence suggests that metabolic processes may be influenced by specific types of exercise and diet. The incidence of obesity seems to be particularly high in populations whose diet is high in fat and whose level of physical activity is low. The trend toward obesity is so pronounced as to suggest that the combined effects of a high fat diet and lifestyle providing for limited physical activity could be synergistic factors in the pathogenesis of obesity.

The difficulty in maintaining an even balance between energy intake and expenditure under these conditions is related to the fact that the caloric density of food is most markedly increased by fat content. If, in addition, energy expenditure is only rarely driven above the resting rate through exercise, the energy balance will all too often become positive. The role of physical activity in maintaining stable energy balance is attributed primarily to the increase in energy expenditure; however, exercise also develops muscle mass and, hence, body cell mass, which will increase metabolic expenditure even under resting conditions.

Considerations such as the above deal only with the balance between energy intake and energy expenditure; as such, they fail to deal with another important aspect of the problem: the fuel metabolized over 24 hours must be the same as the respiratory quotient of the food ingested if body composition as well as energy content is to remain steady. Failure to satisfy this condition is likely to generate food intake signals seeking restoration of a component used in excess if its depletion can be perceived by the organism.

To address this aspect of the problem, it is convenient to use the concept of the respiratory quotient (RQ), which describes the ratio of CO_2

produced to O_2 consumed during the oxidation of various nutrients. When carbohydrate is the only metabolic fuel oxidized, the RQ equals 1.0; when fat is the only metabolic fuel oxidized, the RQ equals 0.7. Measurement of the respiratory quotient makes it possible to determine the relative proportion of carbohydrate and fat being oxidized; by comparing the respiratory quotient to the $CO_2:O_2$ ratio resulting from the experimental oxidation of the mixture of dietary nutrients, which may be called the "food quotient," or FQ, it is possible to assess the extent to which the fuel mixture oxidized by the body differs from the fuel mixture in the diet. If a constant body composition is to be maintained, the RQ averaged over 24 hours must be equal to the FQ.

The typical mixed diet consumed in the United States supplies 45 percent of its calories in the form of carbohydrate, 40 percent in the form of fat, and 15 percent in the form of protein. The FQ for this mixture is 0.85. Since protein contributes only a minor fraction of energy production and since the RQ and FQ are determined primarily by the carbohydrate-to-fat ratio, the effect of protein on these two ratios is small enough to be neglected under most conditions. When this type of diet is consumed, the RQ after an overnight fast in the so-called postabsorptive state is approximately 0.82. This value represents the lowest RQ in the daily cycle, at least for individuals not engaging in prolonged physical work. Because this value is so close to the FQ, it may be concluded that the increase in RQ following the meals must be rather limited. It is interesting to note that the range of likely variations in the RQ resulting from a mixed diet is so limited that knowledge about one key point during the day is sufficient to define the general pattern of RQ variations during the entire day. What this means biologically is that the metabolism of individuals consuming such a diet tends to be locked into a very stable pattern.

The proportions of carbohydrate and fat oxidized in the body are determined primarily by the amount and composition of the food consumed. These proportions can, however, be modified during and following physical activity. Strenuous exercise, for example, which draws heavily on the glycogen reserves of the muscles, is associated with a high RQ. By contrast, sustained physical activity of moderate intensity (aerobic exercise) activates the mobilization of the body's fat reserves, which leads to a gradual decline in RQ. We would like to advance the hypothesis that, to maintain an even energy balance, a certain degree of physical activity is especially useful, if not essential, because it lowers the RQ and thereby helps the organism to operate at an average RQ as low as the FQ of a mixed diet.

Among the three components of food (carbohydrate, fat, and protein), the intake of carbohydrate must be most closely adjusted to its oxidation, and vice versa, because the body's carbohydrate stores are relatively limited (a few hundred grams). Changes in the body's fat reserves, on the other hand, are well tolerated, as evidenced by the ease with which the body adapts to either starvation or excessive accumulation of fat. Protein intake in developed countries is usually far above the recommended daily allowance, but protein accumulation does not occur because the regulation of intermediary metabolism efficiently adjusts amino acid degradation to amino acid intake, thus maintaining a relatively constant body cell mass. Therefore, it is in the carbohydrate sector of metabolism that the most stringent requirements exist for maintaining a close balance between ingestion and oxidation. It is also in this sector that the most powerful regulatory signals governing food intake can be expected.

The notion that carbohydrate ingestion and oxidation must be rather closely matched implies that no appreciable conversion of carbohydrate to fat occurs. Indeed, the presence of even small amounts of fat in the diet strongly inhibits fat synthesis from glucose in experimental animals. It has been established for adult humans that lipogenesis in adipose tissue is negligible, and different lines of evidence indicate that hepatic lipogenesis is also of minor importance when a mixed diet is consumed. Studies of the respiratory exchange following the ingestion of 500 grams of carbohydrate imply increases in the subjects' glycogen stores in excess of 400 grams. Thus, large carbohydrate intake primarily increases glycogen stores without causing an increase in the body's fat content.

When metabolism operates at an RQ higher than the FQ, the fuel mixture consumed contains a higher proportion of carbohydrate than the diet. To recover the oxidized carbohydrate, food must be consumed in amounts exceeding the energy expenditure, which is possible by storing a portion of the ingested fat calories in adipose tissue. Failure to replenish the glycogen stores can be expected to elicit hunger and then to cause a shift in the body's metabolism to reduce carbohydrate oxidation during subsequent hours or days, so as to gradually rebuild glycogen reserves. When metabolism occurs at an RQ below the FQ, a fuel mix richer in fat than the diet is utilized. An energy intake smaller than the amount of energy expended is then required to restore the glycogen reserves.

The importance of exercise in weight control is less than might be believed because increases in energy expenditure due to exercise also tend to increase food consumption, and it is not possible to predict whether the increased caloric output will be outweighed by the greater food intake. By judging the nature of the exercise, using as a criterion its effect on the RQ, it becomes possible to understand how different forms of exercise are more or less helpful in facilitating weight control, weight loss, or even weight gain. For example, the violent exercise performed by the weight lifter is often associated with weight gain in the form of added muscle as well as added fat. On the other hand, sustained exercise such as walking and running leads to decreases in the body's fat reserves, as can be seen in the leanness of long-distance runners. This type of exercise, which has been empirically perceived to be most helpful in achieving energy balance, is often referred to as aerobic exercise. Its special value may be explained by the fact that it leads to RQ values lower than that of the diet.

It follows from the above that a general strategy for facilitating weight maintenance must promote the occurrence of periods in which metabolism operates at a relatively low RQ in comparison to the FQ. Two methods may help to achieve this goal: 1) reducing the fat content of the diet to elevate the FQ; and 2) increasing the type of physical activity, which will depress the RQ.

In response to changes in the proportions of carbohydrate and fat in the diet, the fuel metabolized is rapidly modified. After a few days, the RQ in the postabsorptive state closely resembles the FQ, but physical activity can still cause significant shifts in RQ. In particular, sustained aerobic exercise will gradually bring the RQ toward low values, even if a high carbohydrate diet is consumed.

Futile Cycles

An increase in the rate of synthesis and renewal of cellular storage products and components, if coupled with an equal increase in the rate of degradation, may result in the expenditure of energy without yielding useful work. Thus, the rate of these reversible metabolic steps called futile cycles may determine, in part, the efficiency with which calories are utilized. Little direct information is available from studies in humans to indicate whether these metabolic pathways might be important in the control of energy balance.

Major examples of energy-wasting pathways are the transformations of glucose into and out of glycogen stores and the esterification, deesterification, and reesterification of fatty acids in the fat depot. Unfortunately, evidence is only now becoming available concerning the extent of these processes, which may be substantial under some nutritional conditions (37).

The rate of synthesis and renewal of cell membranes, enzymes, and other cell components is another example of this type of mechanism. Virtually all cellular constituents undergo rapid replacement; as much as 50 percent of an organ is replaced from dietary sources or degradative pools of cellular material every 3 to 4 days. It is now recognized that the turnover of these various components of the body is under a variety of hormonal and nutritional controls. The equilibrium between degradation and synthesis or resynthesis of cellular components in the growing animal must be different from that in the fully mature organism, and the changes in body composition in response to changes in nutrition are different in these two situations. For example, the growth of lean mass continues even in calorically restricted growing animals, whereas this growth does not take place in mature animals. One interesting hypothesis is that alterations in food consumption resulting in caloric intake above or below maintenance levels in the mature organism, which has achieved its genetically predisposed body size and composition, are accompanied by adaptations that tend to maintain the animal's condition. Hormones and nutrition are now known to influence the rate of synthesis and degradation of cellular constituents. The question should now be asked whether changes in these rates induced by altered nutrition or hormonal influences might be responsible for changes in the efficiency of caloric utilization; the answer is not presently obvious. There are few recent studies of over- or undernutrition and the effects of these conditions on energy balance in mature organisms. Most animal studies have been performed in growing animals. In these studies, alterations in energy intake, while producing a gain or a loss of energy in the organism, have required extremely long periods to reach a new, stable weight at the new level of intake. This can be seen as a progressive decrease in net energy retention when expressed as a function of increasing energy intake.

Utilization of Adenosine Triphosphate

At the biochemical level, assuming no change in the state of coupling of oxidation to phosphorylation, changes in the efficiency of calorie usage must be associated with a change in the rate of either formation or utilization of adenosine triphosphate (ATP). Several biochemical mechanisms exist in both plants and animals--including a number of possible mechanisms considered in humans--that may, either alone or in concert, account for changes in metabolic efficiency.

The balance between ATP production and ATP utilization is obviously adjusted precisely because of stoichiometric control. For quite some time it has been possible to calculate the number of moles of ATP produced from the oxidative degradation of carbohydrate, fats, and proteins. Recent experimentation on isolated mitochondria shows that the amount of ATP produced per oxygen molecule consumed may be influenced by altering the ratio of ATP to adenosine diphosphate (ADP) in the surrounding fluid. It seems premature, however, to anticipate that developments in this area will ultimately challenge the presently accepted stoichiometry for ATP production under physiological conditions.

It has been generally assumed that the sodium pump could explain as much as 40-50 percent of basal energy expenditure, but recent studies on energy metabolism in brown adipose tissue have suggested that this may be a considerable overestimate.

Computation of the metabolic costs of different processes, particularly in the course of biosynthesis where the number of ATP needed is known or can be estimated, is often based on $\Delta F'$ value of -7 Cal for the hydrolysis of ATP. Under biological conditions, however, the concentrations of ATP, ADP, and inorganic phosphate (P_i) are such that the hydrolysis of 1 mole of ATP can be expected to liberate 12 to 15 Cal. The best approach to calculating the cost of a process in which 1 mole of ATP is expended is to base it on the total release of energy during the degradation f the substrate, including energy released during nose steps where there is no energy conservation. For xample, the oxidation of 1 mole of glucose liberates 70 Cal and leads to a gain of 36 moles of ATP, or to he release of some 18.1 Cal (approximately 20 Cal) er mole of ATP turned over.

Using the above approach and considering the ninimal ATP expenditure now known to occur in the rocess of lipogenesis from carbohydrate, it can be stimated that some 20 percent of the energy of lucose channeled into lipogenesis is used to cover the TP expenditures needed for fatty acid (FA) ynthesis. This figure is in accord with previous bservations suggesting that overfeeding of carbo-ydrate leads to the deposition of some 80 percent of xcess carbohydrate calories as fat. This is also in ccord with the results obtained in animal studies.

actors Influencing Thyroxine and Reserve Thyroxine iterplay

Overfeeding for 3 to 4 weeks has recently been nown to be associated with an increase in the resting ietabolic rate above that predicted. This increase is milar in magnitude to the decrease commonly found uring periods of fasting. The mechanism(s) esponsible for these changes is not understood; owever, adapting to over- or underfeeding by icreasing or decreasing the metabolic rate clearly has urvival value. The discovery of a diet-induced lteration in thyroid hormone metabolism during both ver- and undernutrition raises the possibility that iese changes might be related to alterations in xygen consumption or rates of cellular turnover. erum concentrations of thyroxine (T_3) are decreased nd those of reverse T_3 (rT_3) increased during fasting, nd similar but opposite changes occur in serum oncentrations of T_3 and rT_3 during overfeeding. It as also been discovered that the carbohydrate content f the diet is important to these diet-induced changes thyroid hormone metabolism. In humans, the hanges produced in T_3 and rT_3 during fasting are mimicked when isocaloric carbohydrate-free diets are provided. Also in humans, the increased T_3 and decreased rT_3 produced by overfeeding can be mimicked by increasing the relative amount of carbohydrate in the diet. In fasting rats, refeeding with carbohydrate and limited protein, but no fat, returns the lower T_3 concentrations found during fasting to normal.

Kinetic techniques have been used to investigate the quantitative significance of these changes in thyroid hormone metabolism. The studies have confirmed a marked increase in the production rate of T_3 during overfeeding and a decrease in the production rate of T_3 during starvation. The biological significance of these alterations, and whether they might be related to the parallel changes in oxygen consumption during over- and undernutrition, is not known at this time. Clearly, further investigations into the interrelationships between nutritionally induced alterations in peripheral thyroid hormone metabolism and metabolic rate are indicated.

Moreover, it has recently been observed that thyroid hormones have a direct influence on mitochondrial phosphorylation and on the rate of sodium pump activity in several tissues. Since a change in the rate of sodium pumping or stimulation of mitochondrial activity would have a significant effect on the energy balance of the entire organism, further investigation into these mechanisms as possible explanations of adaptive thermogenesis seems indicated.

Specific Dynamic Action

There has been increased interest in the effects on energy balance of the specific dynamic action (SDA) of meals, now more accurately referred to as the thermic effect of food. The SDA of food is usually assumed to be roughly 10 percent. The effect of food intake on energy expenditure results, over the course of a day, in a "substrate traffic," whose energy cost may be estimated on the basis of the decrease in energy expenditure at rest during starvation. A similar decrease (about 1 percent per day) has been shown to occur in patients maintained near N balance by consuming 55 grams of protein per day for up to 20 days. It is known that energy expenditure is reduced in individuals deprived of food for prolonged periods, a reduction due, at least in part, to a decrease in the body cell mass. Thus, ingested food probably has an additional and more sustained influence on energy expenditure than does the SDA--the body metabolic rate (BMR) may increase by as much as 20-25 percent in addition to the immediate SDA following the meals. The magnitude and duration of this increased metabolic rate following ingestion may vary, depending on the amount and composition of the calories consumed, the antecedent diet, and the nutritional state of the organism, as well as several other unknown factors. These observations, and the finding by some investigators of an augmentation of this phenomenon with exercise, has led to increased interest and study in this area. Clearly, alterations in the efficiency of this process could have major effects on the overall energy balance of the organism. A great deal more work is required to identify the mechanisms responsible for the thermic effect of ingested food and the possible adaptive responses to it.

Trapping of Calories in Adipose Tissue

It must be realized that the hyperinsulinemia of obesity is a "normal" reaction in a metabolic fuel regulatory system geared toward maintaining homeostasis, because such a system must have the inherent property of seeking a steady state in the absence of food intake. In the presence of increased adipose tissue mass, this steady state is achieved when the release of free fatty acid per kilogram of adipose tissue (FFA/kg) is decreased, resulting in insulin levels higher than normal. It can be calculated from data on FFA fluxes in obesity that, in the fasting state, adipose tissue releases less FFA/kg in obese than in normal individuals. This means that, while the increase in insulinemia due to an increased adipose tissue mass may to some extent be compensated for by insulin resistance, it nevertheless leads to a more intense antilipolytic signal during the postabsorptive state. Since it is generally believed that insulin regulates storage and mobilization of lipid substrates in adipose tissues, and since a meal results in far greater insulin release in obese than in normal persons, the internal environment of obese individuals favors further accumulation of fat deposits.

It seems reasonable to speculate that the trapping of calories in adipose tissue has the same effect on the organism as an increase in energy expenditure or a decrease in food intake, enhancing the signals reaching the food regulation centers, ultimately leading to increased food intake. In other words, to maintain a balance, obese persons need to consume extra calories or, to avoid gaining weight, may have to resist hunger sensations more intense than those experienced by nonobese individuals.

Energy Balance and Body Weight Regulation

Background

There has been considerable factual and conceptual confusion about so-called regulation of body weight. In fact, there is no conclusive evidence in humans to indicate that energy balance is kept constant on a day-to-day basis or even from one month to the next. Furthermore, human body weight and adiposity do not maintain a constant average, but increase slowly with age. Nevertheless, the approximate consistency in weight and adiposity from one year to the next is very closely related to the cumulative quantities of energy taken in and burned.

However, this degree of long-term stability does not, in principle, require a very precise feedback control mechanism. There are a variety of possible stabilizing influences, many of them biologically more plausible than a thermostatlike control mechanism.

Setpoint Concept

The setpoint concept, which theorizes that the body has a tendency to move toward a certain weight or level of adiposity, has frequently been used in discussions of body weight regulation and obesity. Three different uses for the term have been identified:

- As a description of experimental findings which indicate that the body will defend its own weight or fat. In this case, according to one definition, the term "may be valuable as a conceptual convenience, provided it is realized that it does not imply a physiological or structural entity" (157). Alternative terms such as preferred weight level or regulated weight level may also be used. It should be noted, however, that there are different levels or types of body weight defense, but there has been no agreement about which type of defense justifies the use of the term setpoint.

- As reflecting the adaptive value of regulating body fat. In this case, the setpoint concept is used in a functional sense to indicate that body fat is regulated, even if the mechanism involved is only indirectly related to body fat stores.

- As implying a particular type of control system which includes a reference signal representing the ideal level of adiposity for the organism. There is little or no physiological evidence that a reference signal exists for body fat, and it is widely recognized that such a reference point is not needed to achieve body weight regulation. Nevertheless, the control system concept of setpoint may be useful in generating models of weight regulation that can be experimentally tested.

Confusion and unproductive debate can be avoided if investigators using the term carefully specify what meaning they attach to it.

Influence of Food Intake on Resting Metabolic Rate or Hormonal Response

Short-Term Setpoint and Long-Term Equilibrium Point

In this model, the energy flow rate to nonfat tissues when feeding stops is about equal and opposite to the rate when feeding starts. That is, the short-term control system has a preferred value of energy flow (approximately zero), even though the flow is never more than transiently at that value because of the considerable buildup of energy flow toward the end of a meal and the considerable utilization of nonfat energy occurring by the time a meal starts. Thus the short-term control mechanism performs similarly to a closed system with a setpoint or reference value of zero energy inflow into nonfat tissues, although the delays in this "energostat" create large oscillations in energy flow rate. A major long-term control could be merely an equilibrium system, without fixed setpoint characteristics. In this regard, the model is in contrast to the common assumption that short-term control is an open system with a setpoint capable of change, while long-term control is a closed system with a fixed setpoint.

Whether the description of the model's characterizations of long-term equilibrium and short-term setpoint controls proves accurate, this point illustrates the potential value of any detailed analysis of a system. The general terms used to describe the system's behavior often prove to be "chapter headings" for characteristics which are not attributable to any one discrete mechanism but are properties whose generation is distributed diffusely through a number of processes. The most abstract concepts of the present model (e.g., "energy flow") are themselves subject to such reduction in due course. This does not in any way imply that the abstract control characteristics or internal variables do not exist. However, it does imply that there is a limit to the usefulness of repeated demonstrations of functional characteristics by experiments that do not also provide information on the mechanisms by which the functions are achieved. It would be more profitable to elucidate the mechanisms of stabilization of body weight or energy flow than to refine in great detail their setpoint or equilibrium-like properties.

Moreover, current theories of obesity might be more realistic if they used equilibrium-type stabilization concepts. Accounts of the hyperreactivity of moderately obese and some "normal" individuals to strong (and presumably usually external) stimuli do not require a body weight or adiposity setpoint. Any displacement of equilibrium by a decrease in food intake will release a stronger tendency to eat that is monotonically related to distance of fat store size from equilibrium. Furthermore, to the extent that an energy flow deficiency has undifferentiated distress components (as well as components that the subject has learned to ameliorate by eating), restrained subjects will be more reactive to all strong stimuli (arousal or general drive) as well as to strong feeding-related stimuli (specific conditioned drive and incentive). Indeed, when the distinctive distresses of hunger and oversatiation have been poorly discriminated or bias against response to them introduced, this general hyperemotionality will be stronger than in subjects with better detection or lower response criteria, even though these normal subjects may be less reactive to food.

External and Cognitive Controls

It has been argued that fluctuations in human energy balance can be so large and their corrections (whether in part or in whole) so delayed that the observed stability characteristics may be attributed to the individual's perception of his or her own weight or form and his or her deliberate control of food intake and/or energy expenditure.

It has been suggested that the control system is many tiered. Some short-term controls are clear; for example, resting metabolic rate rises and falls with increased or decreased food intake, and hunger and satiety are at least loosely related to recent food intake. These phenomena make it less likely that erratic food intake can change body weight by several kilograms in 1 week, but it is difficult to determine how they contribute to long-term weight stability. Long-term stability may well be achieved mostly through conscious effort. Short-term controls may be sufficient for some individuals to cope with disparity between intake and output, but it seems likely that the majority of people in affluent countries require long-term controls to cope with the energy imbalances their lifestyle imposes.

3

Natural History of Obesity

Lester B. Salans

Obesity is a disorder in which the ingestion of calories in excess of those used by the organism results in excessive expansion of the adipose tissue mass. It is a common condition affecting individuals of all ages in mild to severe degrees. Increasing obesity is associated with increasing health problems. The obese individual is at increased risk for a variety of illnesses; for example, abnormalities in systemic carbohydrate and lipid metabolism are more frequent, including diabetes mellitus, cardiovascular disease, hypertension, and other severe illnesses that significantly affect the quality and length of life. Moreover, obesity may have considerable social, psychologic, and economic impact.

Despite the fact that obesity has long been recognized as a medical and public health problem of major proportions, our understanding of this complex disorder remains poor, and methods of treatment remain inadequate. It is clear, however, that human obesity is not a single disease but a heterogeneous group of disorders. In this respect it is more appropriately considered "the obesities." Only rarely, in perhaps less than 5 percent of cases, can a specific cause of obesity be identified in humans; in the overwhelming majority of obese individuals an underlying cause cannot be ascertained, and specific therapy therefore cannot be determined.

This discussion is concerned with the natural history of obesity, i.e., its pattern and course as it evolves in the lives of individuals in our own culture and time. Knowledge of the natural history of this disorder may provide improved understanding of its etiology and pathogenesis, may bring about new, improved insights into its treatment, and may form the basis for development of public health policy.

Throughout this discussion, however, it must be borne in mind that what we know about the cause of obesity from experience in our own country and time may not necessarily be applicable to other places or periods.

Measurement of Obesity

Since obesity is defined as a state of excessive accumulation of adipose tissue in the body, its diagnosis in strict terms depends upon the demonstration of an increased body fat content. Two basic problems exist in this regard: how to quantitate body fat and how to decide what is "excessive" adiposity. The most objective quantitative methods for estimating body fat content are those which measure total body potassium (^{40}K), total body water with deuterium oxide (D_2O) or tritiated water ($^3H_20$), or body density as determined by underwater weighing (68). Using these techniques, one can estimate the proportion of lean body mass (fat-free mass) as well as body fat, and express the degree of fatness as either the amount of body fat or the percent of body weight as fat.

Although these methods appear to have a firm theoretical basis and to provide a good estimate of adiposity, they cannot be applied on a widespread clinical basis or in public health studies of large populations since they are time consuming and require highly specialized skills and laboratories. Skinfold measurements have proved to be one of the most practical alternative techniques; this method, however, provides useful but less precise information about body fat than the quantitative approaches described above. Several variables limit the accuracy of the skinfold technique, including differences between observers and techniques, and age and sex, particularly in children and the aged (39). To determine the utility and precision of skinfold thickness as a measurement of body fat, the method must be properly standardized and adequately calibrated against the other more quantitative techniques.

Nevertheless, skinfold thickness appears to provide a practical index of adiposity. In most surveys and certainly in most clinical settings, measurements of body weight--corrected for height, sex, and frame size--have been utilized to assess obesity. These measurements provide even less information about body fat and assume that overweight and obesity are synonymous, an assumption which may not always be valid. Furthermore, the use of body weight as an index of obesity is based on a comparison of an individual's weight with so-called desirable, average, or ideal weight as given in a standard table of individuals of the same sex, age, and frame size [19(1):72-76]. There are several questions surrounding these tables, including the manner by which the "standard" data were obtained and the arbitrary definitions of "desirable" and "ideal."

There is also the problem of defining what is a normal or optimal amount of fat in the body, and what is a normal or desirable body weight. Body fat and weight are continuously distributed in populations, with no clear cutoff between lean and obese individuals. Optimal body fat and weight for an individual probably depends upon a variety of factors, including the genetic disposition toward obesity; aggregated diseases such as diabetes, coronary heart disease, hypertension; the nature of the environment, particularly the likelihood of encountering situations such as caloric deprivation or catastrophic stress that require a generous caloric reserve; and psychological comfort and the cultural concept of what constitutes an appropriate body size. At present, however, there is little quantitative information upon which firm conclusions about "optimal" body fat or weight can be based.

The proportions of body weight as fat generally accepted as being "normal" are 15-20 percent for men and 20-25 percent for women. In contrast, obese individuals may have as much as 50 percent of their body mass as adipose tissue. Deviations in body weight from the standard tables are usually expressed as percentage overweight; 10-20 percent overweight is generally considered to be indicative of obesity, while deviations of lesser degree may reflect increased adiposity and/or increased lean body mass. More definitive data are required on the body composition, both lean body mass and body fat, of overweight and obese individuals of all ages.

Natural History of Obesity

Almost all the available information on the prevalence and natural history of obesity in our society is derived from surveys measuring body weight in relation to height and age to determine obesity. In light of the preceding discussion, the resulting data should be regarded as more qualitative than quantitative.

Long-term surveys in which the body weights of a number of individuals are followed for substantial portions of their lives appear to provide the most information about the natural history of obesity, but such studies are difficult, extremely time consuming, and susceptible to bias. Groups of people studied in this fashion are not likely to be representative of an entire population, and there is great difficulty obtaining followup observations over a number of decades for a high percentage of the sample. Furthermore, the subjects' knowledge that they are being observed may distort their behavior and thus the natural history of the disease. Most of the current information about the cause of human obesity comes from a large number of cross-sectional studies of body weight in various populations. While these do shed light on the natural history of obesity, they reflect only a cross section of the population; and the conclusions are, therefore, necessarily limited.

Information on the natural history of obesity based on published long-term surveys and cross-sectional studies of body weight is fragmentary and often confusing, as summarized in the following paragraphs.

Obesity is a common condition that appears to be increasing in frequency. Current estimates of its prevalence are highly variable, and its exact incidence in the population is unknown, a foreseeable fact since the evidence is based entirely on measurements of body weight in relation to height and age. As previously discussed, in these surveys overweight and obesity have been considered synonymous, a relationship which may not always hold true. Nevertheless, even with the most cautious interpretation of the available data, the extremely frequent occurrence of overweight/obesity at all ages and in both sexes of our population is impressive. Moreover, the prevalence appears to be increasing; American adults, both males and females, examined during the period 1971-74 have been found to weigh more than those studied in 1960-62, a change which cannot be attributed to a corresponding increase in height (116). Similar observations have been made in several other developed countries.

Obesity affects individuals of all ages, from infancy to old age. It increases in frequency from young adult life to middle age, but whether it is more frequent in later life depends on whether allowance is made for the reported decrease of lean body mass with aging. If this is taken into account and obesity is defined on the basis of the percent of body weight as fat, obesity would appear to increase in frequency throughout the life of the population. Whether increased obesity with age is an inevitable concomitant of the aging process or the product of a sedentary culture is not yet clear.

Several studies indicate that obese infants are likely to become obese children and adults (2,31). The study of one population indicated that 80 percent of the obese children became obese adults and that 50 percent of the very obese adults had been obese infants. The prognosis for children with milder degrees of obesity is unknown, although it has been reported that infant weight correlates closely with adult obesity independent of parental weight, socioeconomic status, and educational level. There are, however, conflicting data (124). Studies from England indicate that the majority of fat babies lose their excess fat during childhood and that, while obesity in infancy may have some influence on obesity in childhood, it is small and only one of many factors determining later weight. Although it seems clear that infants and children with severe obesity have a poor prognosis and are very likely to become obese adults, the extent to which obesity of infancy and childhood is an important reservoir of obesity in adult life remains to be clarified. Studies are also required to document the relationship of overfeeding and rapid weight gain in infancy to obesity in adult life.

Once established, obesity is difficult to reverse, particularly when the goal is permanent maintenance of normal body weight. The trend toward continued lifetime obesity appears to be somewhat stronger among women than among men. The concept has been generally advanced that early-onset, massive obesity is more resistant to therapy than adult-onset, mild obesity; this remains to be documented.

Obesity is believed to be associated with increasing morbidity from a variety of disorders including glucose intolerance, hyperinsulinemia, hyperlipoproteinemia, diabetes mellitus, cardiovascular dysfunction, coronary heart disease, hypertension, and pulmonary dysfunction, to name but a few. The degree and character of these associations have not been well documented, however, i.e., whether the risk of a given disorder increases in proportion to excess weight, whether there is increased risk for all degrees of obesity, whether risk increases only after a certain level of obesity is attained. Evidence is also lacking concerning the relative contribution of obesity per se (increased adipose tissue) and other bodily constituents involved in overweight, such as lean body mass, to the risk of developing these disorders. Finally, in only some of these disorders is there evidence that weight loss and reduction of adiposity is accompanied by improvement in the associated condition.

Contributing Factors

While genetic, metabolic, endocrinologic, and nutritional factors are important determinants of obesity, epidemiologic data indicate that the prevalence and course of human obesity is strongly influenced by social, economic, racial, and ethnic factors (56). These data demonstrate that obesity is far from being uniformly distributed within our society; it is, for example, highly prevalent among middle-aged women of low socioeconomic status, and in certain racial and ethnic groups. It is possible that this uneven distribution of obesity is a reflection of different underlying attitudes toward eating and obesity in the different strata of our society. Certainly, the degree of fatness, and therefore the proportion of obese individuals in a population, would appear to be determined by food availability and cost, at least up to a point. Available evidence indicates that after that point, social and cultural factors may be important contributors to the development and course of obesity. In Westernized cultures, there is an inverse relationship between the level of fatness in the adult female and the levels of education, income, and occupation. Even in cultures where female obesity was formerly admired, Westernization--bringing with it television, movies, and jeans--now tends to reduce the level of fatness in the most affluent female.

Within populations, fatness clearly follows family lines; obese parents tend to generate obese children, and an obese propositus (index case) tends to have obese siblings. It is impressive to observe that as they age, the children of the obese become increasingly fatter than those of lean parents. Before accepting a genetic explanation, however, it is important to realize that exactly the same trends take place in adopted children of obese parents and in genetically unrelated adopted siblings of obese propositi (57). There is evidence, moreover, that obese mothers have more children than do lean mothers. The net result is that obese people reproduce faster, and if this trend continues, the prevalence of fatness is bound to increase.

The apparent effects of socioeconomic factors on the level of adiposity can be seen in early life. In the United States, low income or poverty-level boys and girls have been shown to be leaner than median-income boys and girls, but fatter than children in the highest socioeconomic status (SES) categories. The same generalization applies to low-SES, adult American males and females. In adults of both sexes who are truly affluent and truly below poverty level, obesity is again less common. Upward socioeconomic mobility is associated with decreasing risk of obesity, while the opposite is true for downward mobility. Surveys in the United Kingdom indicate that, although obesity is more common among lower SES male and female Londoners than among higher SES groups, the prevalence of obesity is quite low among men engaged in heavy manual labor (135). Therefore it is clear that, although there appears to be an association between obesity and SES, it is neither linear nor straightforward. The nature of this relationship and the specific social factors responsible for it--income, education, psychologic, etc.--need further elucidation.

A correlation between obesity and certain racial and ethnic groups has also been reported. Black women are at greater risk than white women. But the reverse is true for male adults; white men suffer more obesity than do black men. Thus, the nature of the relationship between race and obesity remains to be defined. In this regard it should be noted that differences between races disappeared when the groups were of the same socioeconomic level. Similarly, although factors such as ethnicity and religious affiliation have been linked to obesity, these relationships have not been well documented. It is clear that there is a need for detailed epidemiologic studies of well-defined racial and ethnic groups in the United States, as well as in other affluent and less affluent countries.

Some obese persons resist weight reduction, sometimes subtly and sometimes overtly, because they feel their size is appropriate or, perhaps, only a few pounds over a desirable weight. Cultural factors operating in social groups or within a family may determine opinions on what constitutes an appropriate body weight. These cultural attitudes may also influence what is regarded as the proper composition and size of meals. Some generations and some cultural groups feel more strongly than do others that their pleasures should not be denied, and the enjoyment of food may become an important part of their lives.

Pregnancy commonly causes weight gain that often continues after delivery; successive pregnancies frequently cause further increases. This phenomenon may be endocrine in nature, but it also may result from a number of other interrelated psychosocial factors. One such factor may be the belief that a pregnant woman must "eat for two"; another may be the restriction of the mother to the home after delivery to care for the child, thus reducing physical activity and increasing eating for pleasure to compensate for limited personal activities. Whatever the explanation, pregnancy is a common precursor of obesity, and the reasons for this are not yet understood.

The association of obesity with multiple psychological problems is well recognized and has been exhaustingly researched and reviewed (92). Psychological disturbances may cause obesity, may be the result of obesity, or may even be the consequence of weight loss. While emotional disturbance is a frequent precipitant of overeating, and hence obesity, it is by no means a factor in all cases; the majority of obese subjects are no more prone to emotional disturbances than are the nonobese. However, it has been suggested that when emotional factors do assume importance, they are probably a result of faulty associations in childhood. Perceptual factors have also been implicated in the development and course of obesity; it has been suggested that obese subjects are less able than nonobese individuals to perceive internal feeding cues and, as a result, eat only in response to external cues such as the sight of food. The emotional burden of being fat in a society that rewards leanness and stigmatizes obesity can be enormous. It is no wonder, then, that obese persons suffer frequent and varied psychological disturbances, ranging from mild to severe.

It is clear from the preceding discussion that social, economic, cultural, and psychological factors may be important contributors to the development and course of human obesity; in other words, obesity is influenced by lifestyle. The degree and character of these relationships need to be documented and analyzed in detail if our understanding of obesity is to be improved and if more satisfactory approaches to its treatment, prevention, and cure are to be developed.

Recent Research Findings

Recent basic and clinical studies of humans and laboratory animals have provided some new insight into the natural history of obesity and its associated metabolic abnormalities. Some of these advances are summarized in the following paragraphs.

Anatomic and Metabolic Alterations in Human Obesity

Examinations of the anatomic alterations that account for expansion of the adipose tissue mass and of the systemic and cellular metabolic alterations which accompany this expansion have begun to provide an understanding of the physiological basis for the clinical course of human obesity (83, 131).

Morphologic Development of the Adipose Tissue Mass in Obesity

The size of the adipose tissue mass at any one time, whether during growth or in adult life, is the product of the number of adipose cells and the amount of triglyceride (TG) per cell (adipose cell size). The recent development of reliable methods for determining the mean size of adipose cells in isolated pieces of adipose tissue and for estimating the total number of adipose cells in the body has permitted detailed study of the cellular character of adipose tissue in both nonobese and obese individuals. Such studies indicate that the adipose tissue normally grows by an increase in adipose cell size during the first year of extrauterine life, the majority of adipose cells presumably being formed in utero. After the first year, much of the enlargement of adipose tissue occurs as the result of an increase in adipose cell number, although cellular enlargement probably makes a contribution. Recent data suggest that adipose cell size may be an important factor in the regulation of adipose cellular replication, and that whenever a given maximum cell size is attained, replication of adipose cells occurs (90).

Studies of the cellular character of the adipose tissue of obese humans indicate that expansion of this tissue is achieved either by an increase in adipose cell size (hypertrophic obesity), or by an increase in both adipose cell size and cell number (hypertrophic-hyperplastic obesity). Adipose cellular enlargement, but not hypercellularity (an abnormal increase in the number of cells), is common to all types of obesity. The existence of adipose hypercellularity in humans apparently depends upon two factors: the severity of obesity, and the subject's age at its onset. When body weight exceeds 170 percent of ideal, a maximum cell size (1 to 1.2 micrograms TG per cell) is apparently reached; thereafter, cell number and obesity are highly correlated (83). In addition, hypercellular obesity in humans most often has its onset in early life, usually before the age of 20 years; obesity of later onset is usually, but not always, accompanied by adipose cellular enlargement but not by an increase in cell number (131). Hypercellularity seems most likely to occur at two periods in early life: within the 1st year, and at or around the time of puberty. Thus, extreme obesity beginning at any age can result in adipose hypercellularity, but such replication seems particularly likely in infancy and puberty.

Although hypercellular obesity in humans usually occurs early in life, some individuals with apparent adult-onset obesity have been reported to have increased numbers of adipose cells (83). Whether this reflects actual formation of new adipocytes in adult life or merely lipid filling of preexisting adipocytes awaits clarification. Similarly, hypercellularity is not limited to patients with severe obesity. Increased adipose cell numbers have been observed in some individuals suffering only moderate degrees of obesity; in these individuals obesity almost always begins in early life.

The relevance of these observations to the understanding of the natural history of obesity becomes more apparent when one considers the additional observation that weight loss and reduction of the adipose tissue mass in all adult obese patients, regardless of age of onset or degree and duration of obesity, have so far been shown to be accompanied by a change in adipose cell size alone; cell number remains constant even in the face of massive weight loss. Even in children, decreases in body fat are accompanied by a reduction in adipose cell size without significant change in the total cell number (98). An exception to this--a case in which weight loss was accompanied by a reduction in cell number--has been reported in a study of obese children under age 6, in whom total cell number had not yet exceeded adult values.

The bulk of the evidence supports the concept that, once established, adipose hypercellularity in the patient with early-onset, massive obesity is irreversible. This morphologic phenomenon parallels the well-recognized and frustrating clinical course of the disorder in which the lifelong, severely obese patient is intractable to treatment. Furthermore, the observation that adult-onset obesity is primarily associated with the reversible alteration of adipose cellular enlargement provides a basis for the postulated but as yet undocumented hypothesis that this form of obesity is more amenable to treatment. Further studies are required to determine if and how the number of adipose cells an individual has influences the course of his disease and its metabolic consequences.

While the classification of obesity as hypercellular or hypertrophic on the basis of the morphology of the adipose tissue appears to be reasonably well founded and a rational explanation for the developmental processes leading to these alterations in the adipose tissue mass is nearly at hand, several major questions persist. Foremost is the specific relationship between the cellular character of the adipose tissue mass and the regulation of eating behavior, energy balance, and body weight; long-term studies demonstrating that hypercellularity early in life or during the "critical periods" (e.g., in utero, 1st year of life, puberty) actually leads to adult obesity are presently not available. Conversely, the roles of a variety of factors in the development of obesity and their influence on the mechanism of adipose tissue expansion remain controversial; these factors include genetics, maternal weight gain or loss, early infant and childhood feeding and obesity, and early metabolic and endocrine alterations. Finally, the relationship between the character of the adipose tissue mass in obesity and the clinical reversal of this increasingly common condition is yet to be established.

Metabolic Consequences of Obesity

Diabetes mellitus and insulin resistance. The close association between obesity, abnormal carbohydrate metabolism, and diabetes mellitus has been recognized for many years, but the nature of this relationship still remains poorly understood. In some patients obesity appears to be part of the syndrome of diabetes mellitus, but in many instances obesity seems to be acting as a primary factor, somehow inducing abnormalities in carbohydrate metabolism and insulin secretion which may or may not be manifestations of the diabetic syndrome. Weight loss by obese patients is usually associated with an improvement in hyperinsulinemia and often restores normal glucose metabolism, thus supporting the concept that in these individuals obesity is an aggravating rather than an associated factor. The National Commission on Diabetes has reported that the factor most strongly associated with the prevalence of adult-onset diabetes in the United States is the degree and duration of obesity (117).

Obesity is associated with increased rates of pancreatic insulin secretion and increased concentrations of insulin in the blood, both in the basal state and in response to glucose. The explanation most commonly advanced for this is the existence of "insulin resistance," i.e., the decreased ability of insulin to influence glucose uptake and metabolism in the insulin-sensitive tissues of obese individuals: the liver, skeletal muscle, and adipose tissue (130). It is postulated that insulin resistance in these tissues leads first to hyperglycemia and second to hyperinsulinemia. Indeed, an impairment in insulin action has been observed in adipose tissue, muscle, and liver from obese patients. The tissue with the principal role for regulating glucose homeostasis is the liver; hence a defect in this tissue could be responsible for the hyperglycemia of obesity. The nature of the tissue defect responsible for insulin resistance--whether it resides in alterations in the interaction of insulin with its specific cell membrane-located receptor, in glucose transport, or in some intracellular metabolic function--remains to be determined. Recent studies indicate that, in certain types of obesity, the number of cell membrane-located specific insulin receptors is decreased in adipocytes and circulating monocytes. Other studies, however, report that impairment in insulin action on glucose metabolism by adipose cells from obese patients is not associated with a decrease in insulin binding or receptors, but rather with an alteration in intracellular glucose metabolism, which may not be under the direct control of insulin. Although an explanation for this apparent discrepancy remains to be found, it is possible that these differences reflect different types of obesity.

If tissue resistance to insulin is an important factor in the development of hyperinsulinemia, the mechanism by which this resistance is "read out" by the beta cell of the pancreas and by which insulin secretion increases has yet to be identified. Hyperinsulinemia is often observed in obese patients in the absence of hyperglycemia, suggesting that factors other than, or in addition to, blood glucose concentration may be involved. For example, increased concentrations of branched-chain amino acids have been observed in obese patients, and it has been proposed that this hyperaminoacidemia stimulates the beta cell to secrete excess insulin (44).

Other primary signals have also been postulated, but remain to be identified.

On the other hand, it has been suggested that the hyperglycemia and hyperinsulinemia of obesity are not the consequence of tissue insulin resistance, but the result of overeating. According to this theory hyperinsulinemia is the result of the ingestion of excessive numbers of calories, particularly in the form of carbohydrate, and as a consequence of chronic exposure to high levels of insulin, the tissues become less sensitive to insulin action. It has further been suggested that chronic hyperinsulinemia exerts negative feedback on the specific insulin receptors in the cell membrane, the so-called "down regulation" of insulin receptors in which, as an adaptation to high levels of insulin, the number and availability of specific receptors to bind insulin is reduced. The observed alteration in insulin's ability to influence glucose metabolism in the peripheral tissues, then, is considered to be a secondary or adaptive phenomenon, serving as a protective mechanism against hypoglycemia in the face of hyperinsulinemia.

Whatever the mechanism, it is clear that obesity imposes a burden on glucose metabolism and insulin secretion. Thus, obesity is a diabetogenic factor.

Hyperlipoproteinemia and hypercholesterolemia. An association between obesity and hyperlipoproteinemia has also been observed, suggesting that obesity may influence lipid metabolism (118). Elevations of plasma triglyceride and/or serum cholesterol levels have been reported to be common in obese patients. The best studied and clearest association to date is between obesity and hypertriglyceridemia. One as yet unproved hypothesis advanced to explain this association is that the hyperinsulinemia of obesity results in accelerated hepatic triglyceride synthesis and, consequently, elevated plasma triglyceride in the form of very-low-density lipoprotein. However, since hypertriglyceridemia is not present in all patients, obese or nonobese, with insulin excess, and since not all obese patients with hyperinsulinemia demonstrate hypertriglyceridemia, other factors are clearly involved.

Obesity has been less closely associated with increased plasma levels of cholesterol. Endogenous cholesterol production is enhanced in obese individuals, and this may be responsible for the increased serum cholesterol concentration and increased risk of cholesterol gallstones in obese individuals. The factors responsible for the increased cholesterol production and hypercholesterolemia remain to be identified.

Animal Models in the Study of Obesity

Animal models are available for exploring the etiology and consequences of obesity, as well as potential modes of treatment; many of these studies are not possible in humans. Several varieties of obese laboratory animals have served as extremely useful models for the study of human obesity, particularly for defining the details of adipose cellular development and of metabolic interrelationships in obesity (24). Although the availability of such models increases the number and variety of studies that can be undertaken, the extrapolation of experimental results to human obesity must be made with extreme caution and only as the appropriate confirmatory studies in humans can be carried out.

Growth and Development of the Adipose Tissue Mass in Obesity

Details of the course and timing of the cellular events that determine normal growth and development of the adipose mass have been better defined for rats and mice than for humans, largely because of the ability to administer ^{3}H-thymidine to laboratory animals and to measure its incorporation into adipocyte DNA over time (83). One of the primary difficulties in interpreting human cellular data is that satisfactory methods do not exist for detecting presumptive fat cells which contain little or no lipid, i.e., the preadipocyte or small cell from which most or all lipid has been lost due to weight reduction. Measurement of incorporation of labeled thymidine into adipose cellular DNA of rats and mice has been extremely useful in this respect. Combining this technique with the measurement of adipose cell size and number has permitted a detailed description of adipocyte development in several nonobese and obese rodents through the stages of cellular differentiation, proliferation, maturation, and lipid filling.

Strong evidence that early life is a critical period for adipose cellular development and that there is a fixed number of adipose cells in the mature organism comes from studies of adipose cellularity in rodents subjected to differing nutritional conditions at various stages of life. (The epididymal fat depot is commonly used in these studies as a convenient source of fatty tissue.) Various manipulations induced during postweaning and adult life, such as severe acute starvation, chronic malnutrition, and hypothalamic-induced hyperphagia and obesity produced no lasting effects on adipose cell number in the adult animal; only cell size was affected. Malnutrition from 6 to 12 weeks postpartum seemed to halt cell number increases, but upon refeeding, cell number returned to normal. There was a lasting reduction in cell number compared with ad libitum-fed controls only when manipulation occurred during the preweaning period; e.g., under- and overnutrition of newborn rats during the first 3 weeks of life produced permanent changes in adipose cell number in the adult animal, even when the adult was allowed free access to food (99). These studies have been interpreted to mean that final adipose cell number is determined in the epididymal fat depot very early in life; when it is attained, no further cell addition or deletion occurs, and only fluctuations in cell size are possible.

This concept of a fixed, unchangeable number of adipose cells in adult life and of the existence of a critical period of adipocyte proliferation during early life when cells are particularly sensitive to their environment has been challenged by several investigators (38, 88:20-27, 102, 141). It has been reported that feeding large amounts of fat, particularly to certain susceptible strains of rats, will result in increased adipose cellularity in some, but not all, adipose depots. Similarly, exposing rodents to cold temperatures has been reported to produce such changes. Moreover, overfeeding obese rats induces adipose cellular enlargement until a maximum cell size is attained; further increases in adiposity are associated with increasing cell number alone. It remains to be determined whether such changes in cellularity reflect actual new adipose cell differentiation and proliferation or the fat filling of preexisting but lipid-empty preadipocytes. In any case, the fact that only some species respond with increasing cellularity, and in only some depots, points out that a complex interaction of genetic endowment, environmental conditions, and developmental stage is involved.

As is the case with humans, obesity in experimental animals can be classified on the basis of their adipose tissue as hypertrophic (increased cell size, normal total cell number) or hypertrophic-hyperplastic (increased cell size and number) (83). In most instances, there appears to be a close relationship between the cellular pattern of the adipose tissue and the subject's age at the onset of obesity. Obesities, such as genetic obesity, that are manifest in rodents at early ages are found to be a mixed hypertrophic-hyperplastic type. Obesities that occur later in life, such as those produced by hypothalamic lesions, by forced feeding, or even by genetic influences acting at a later age, are exclusively hypertrophic. An exception to this relationship appears to reside in obesity induced experimentally in adult rats and mice fed high-fat diets for prolonged periods. These animals have been shown to increase adipose cell number in association with their gain in body weight; however, it remains to be determined whether this increase in cell number reflects new cell formation or lipid filling of preexisting lipid-empty preadipocytes.

The Zucker obese rat, an animal with mixed hypertrophic-hyperplastic obesity, has been studied in great detail. This animal appears to have a genetically determined failure to regulate adipose cell proliferation and/or differentiation in early life, an abnormality which increases the predisposition to hyperplastic obesity. The finding of an enhancement of lipoprotein lipase (LPL) activity occurring during early normal development prior to changes in fat cell size and the demonstration that LPL is elevated in preobese rats suggest that disruption of the normal developmental sequence of adipose tissue mass regulation may well occur at the level of control of differentiation (90, 141). This possibility once again focuses attention on early life and the potential existence of "critical periods" during the growth of the adipose tissue during which the actively differentiating and proliferating adipose organ is particularly sensitive to factors which influence cellular differentiation and division. Obvious factors for consideration include those of nutritional, endocrine, metabolic, and genetic origin. Much work remains to be done to elucidate this entire area in our effort to understand the causes and course of obesity.

Potential Causative Factors in Obesity

The abnormalities that occur in most animal models of obesity have similarities in their overall development. However, the involvement of many factors and different genes in each of the various types of obesity makes it unlikely that the causes will be reduced to a single defect. Hyperphagia and hyperinsulinemia appear to be two key factors in the development of obesity in most, if not all, experimental animals studied to date; development of obesity in rodents, regardless of etiology (e.g., dietary, hypothalamic, genetic), is associated with varying degrees of both these conditions. Whether hyperphagia or hyperinsulinemia is the initial event has not been determined in each of the various animal models of obesity; the two are closely interrelated, and each may lead to the other. If the neonatal or adult animal, for whatever reason, fails to develop normal satiety mechanisms, it may become hyperphagic, develop hyperinsulinemia, and ultimately become obese. On the other hand, it may be that primary hyperinsulinemia, for whatever reason, produces hyperphagia during and/or after the neonatal period and, hence, obesity. If this is the case, a vicious cycle of events would be established, characterized by beta cell hypertrophy/hyperplasia, hyperinsulinemia, hyperphagia, obesity, and an insulin-resistant state. The ultimate condition, either massive obesity or diabetes, would depend on the ability of the beta cell to respond to the continuing demand for increased insulin.

Early studies have demonstrated the primary role of the hypothalamus in the regulation of food intake. Electrolytic lesioning in the VMN region of the ventromedial hypothalamus has been shown to lead to hyperphagia and obesity, whereas lesioning of the lateral hypothalamus (LH) leads to aphagia, loss of weight, and death by starvation. These studies have led to the concept of the VMN region (satiety center) as the modulator of the LH (feeding center) food intake regulation. Further studies in experimental animals have established that hyperinsulinemia is essential to the development of obesity (9). Indeed, recent evidence in rats indicates that destruction of the ventromedial hypothalamic nuclei may produce hyperinsulinemia and enhance lipid synthesis in the adipose tissue even in the absence of hyperphagia. Severing the vagus nerve prevents hyperinsulinemia and hypothalamic obesity, further establishing the essential role of vagal stimulation of the pancreas to the development of obesity.

Like human beings, adult laboratory animals supplied with highly palatable food ad libitum--particularly food high in either glucose or fat content--become hyperphagic, hyperinsulinemic, and obese, alterations which are reversed upon return to conventional food. Studies of these dietary obesities may provide useful insights into the nature of relationships between hyperphagia, hyperinsulinemia, and obesity.

Genetic obesity has also been well studied (24). Massive obesity is caused by the independent action of several different single genes. Detailed studies of these single gene mutations have led to considerable insight into possible mechanisms in the production of obesity. Four mutations--obese (ob), diabetes (db), agouti (A^{vy}), and fat (fat)--at four loci cause obesity and diabetes-like syndromes in mice, whereas one mutation--fatty (fa)--causes obesity in rats. The New Zealand Obese (NZO) strain of mice provides a model of mild-to-moderate obesity, caused by several genetic factors. These animals are all both hyperphagic and hyperinsulinemic. The primary defect in the genetic diabetes (db/db) mouse probably involves a defective satiety center that prevents it from recognizing satiety cues (35, 59). In contrast, the phenotypically identical obese (ob/ob) mouse appears to have some defect in the production of sufficient or effective satiety factor(s), and remains hyperphagic and becomes obese. Primary defects of the B cell (as suggested for the fatty rat) causing B-cell overresponsiveness to insulin-releasing stimuli would produce hyperphagia and obesity identical to those in models with primary satiety defects. Other primary defects may involve the fat cell itself, such as more efficient utilization of calories to produce fat (NZO mouse). Still other models may be able to make metabolic adaptations to utilize food more efficiently, thereby producing excess fat even when the subject eats normal amounts.

Altered Metabolic Function in Obesity

In an attempt to gain insight into the factors responsible for, and the nature and course of, the abnormalities of carbohydrate and lipid metabolism so frequently associated with obesity, several researchers have undertaken detailed metabolic studies of various animal tissues.

Adipose tissue and cells. In general, the metabolism of glucose in adipose tissue fragments obtained from laboratory animals and humans can be directly related to the number of adipose cells in those fragments. At the same time, however, several parameters of glucose metabolism in this tissue are influenced by the size of its constituent cells (130); cell size-related alterations in metabolic function can be observed in both intact adipose tissue and isolated adipose cells. When adipose tissue is obtained from rats ingesting diets of similar carbohydrate, fat, and protein composition, and during similar growth states, increasing adipose cell size in the absence of insulin is associated with unchanging rates of glucose oxidation, increasing rates of glucose carbon incorporation into triglyceride glycerol, and decreasing rates of de novo fatty acid synthesis from glucose. On the other hand, the stimulation of each of these metabolic parameters by insulin decreases with adipose cellular enlargement when studied under these same conditions. This parallels some of the reported observations in human adipose tissue.

The lipolytic character of adipose tissue appears to be influenced also by the size of its constituent adipose cells. The basal rate of lipolysis (glycerol release) in isolated rat adipose cells increases with increasing cell size and is paralleled by increasing fatty acid release in the absence, but not in the presence, of glucose; a progressive elevation of cell-associated, presumably intracellular, nonesterified fatty acids (CAFA); decreasing rates of de novo fatty acid synthesis from glucose; and increasing capacity for reesterifying preformed fatty acids. In the presence of epinephrine, increasing adipose cell size is accompanied by increasing lipolytic activity, increasing net triglyceride mobilization, and increasing intracellular fatty acid levels. The net lipolytic effect of increasing cell size, then, is an increase in the efficiency of lipolysis and a relative decrease in reesterification. It should, however, be noted that the enlarged adipose cell is less sensitive than the small cell to the effect of epinephrine.

Increasing adipose cell size in the rat is also accompanied by a decreasing antilipolytic effect of insulin. The association between adipose cellular enlargement and increasing basal and epinephrine-stimulated triglyceride turnover is, therefore, paralleled by both a decreasing response to and a decreasing antilipolytic effect of insulin. Increasing CAFA levels accompany all these cell size-related metabolic alterations.

The decreasing lipogenic and antilipolytic responses to insulin with adipose cellular enlargement are presently the subject of intensive investigation; to date, attention has been primarily focused on the altered capacity of insulin to stimulate glucose metabolism in the enlarged adipose cell. Each of the as yet hypothetical steps in the mechanism of insulin action--binding to receptor, stimulation of glucose transport, and enhancement of glucose metabolism--has been examined in isolated adipose cells as a function of increasing adipose cell size (130).

Specific equilibrium insulin binding to the enlarged adipose cells of genetically obese mice is reportedly decreased relative to binding to the smaller cells of lean controls. A similar finding of decreased insulin binding to the enlarged adipose cells of old, obese male rats has been reported from one laboratory. However, more recent studies have failed to demonstrate any reduction in equilibrium insulin binding to adipose cells isolated from aging obese rats; on the contrary, increasing adipose cell size in these animals appears to be associated with increasing insulin binding. Increasing insulin binding per cell, therefore, may not parallel and may not explain the decreasing metabolic response to insulin seen with increasing adiposity.

Preliminary studies of glucose transport activity in adipose cells indicate that increasing rat adipose cell size is associated with increasing basal and submaximally insulin-stimulated glucose transport activity, proportional to the cell's expanding surface area; maximally insulin-stimulated transport activity, on the other hand, remains roughly constant on a per-cell basis. In the presence of physiological glucose concentrations, then, the enlarged adipose cell's capacity for glucose transport far exceeds the quantities of glucose actually taken up and metabolized, suggesting 1) that alterations in glucose metabolism beyond transport must be responsible for the decreasing rates of insulin-stimulated glucose utilization with increasing adipose cell size, and 2) that glucose transport activity may not represent the rate-limiting step in glucose utilization in the enlarged adipose cell of older animals. Moreover, these studies fail to demonstrate alterations in the sensitivity of glucose transport to insulin.

Studies of the concentration-dependent stimulation of several parameters of glucose metabolism by insulin provide further evidence for metabolic alterations beyond the glucose transport step in adipose cells of increasing size (44). Adipose cell size does not affect the sensitivity of rat adipose cells to the stimulation by insulin of glucose oxidation, de novo fatty acid synthesis from glucose, and glucose carbon incorporation into triglyceride-glycerol. The decreasing maximal response to insulin in the absence of altered sensitivity to hormone concentration reflects an effect of adipose cellular enlargement on the cell's capacity for glucose metabolism and not on the mechanism of insulin action.

The alterations in adipose cell function observed in vitro with increasing cell size are paralleled by similar alterations in the systemic metabolism of carbohydrate and lipid in the whole animal. Thus, at a time when an impairment in the ability of insulin to influence glucose metabolism in the enlarged adipose cells of obese rats is observed in vitro, the ability of insulin to influence glucose metabolism in the whole organism is also impaired, as reflected in glucose intolerance and hyperinsulinemia, and a decreased hypoglycemic response to insulin. Weight loss, in turn, is associated with an improvement in glucose tolerance and a fall in plasma insulin concentrations, concomitant with a restoration to normal of the in vitro metabolic character of the adipose tissue and a reduction in adipose cell size. Thus, the alterations in carbohydrate metabolism and insulin action are not primary abnormalities of obesity per se, but are secondary to the natural course of obesity. Similar observations have been made in humans, as discussed earlier. In addition, the increasing in vitro rates of lipolysis and triglyceride turnover and the shift from glucose lipogenesis to preformed fatty acid uptake and esterification with adipose cellular enlargement may lead to an increase in systemic fatty acid flux and hypertriglyceridemia.

Muscle and liver. In view of the fact that the liver and, to a lesser extent, skeletal muscle are the most important tissues controlling the glucose homeostasis of an animal and that these tissues rather than adipose tissue are most likely to be directly responsible for the altered state of glucose metabolism in obesity, detailed metabolic studies of liver and muscle are needed. To date, only limited research on these tissues has been undertaken in laboratory animals. Of interest, however, is the observation that, in studies of the effects of fasting and feeding on the tissues of the ob/ob mouse, the relationship between insulin binding and metabolic effects of the hormone is not identical in all tissues. Insulin binding and effect on glucose metabolism changed in a parallel manner, but were divergent in both muscle and adipose tissue, indicating again that a multiplicity of factors may be responsible for alterations in cellular glucose metabolism. The investigations of the adipose tissue described above serve as an excellent model for metabolic studies in other tissues.

Dietary factors. The diet of the obese individual is excessive not only in total calories but also in carbohydrate and fat; the profound influence of both the quantity and quality of calories on systemic glucose metabolism and insulin secretion is well established. The altered glucose metabolism and hyperinsulinemia of obesity are, therefore, possibly a consequence of these dietary factors rather than, or in addition to, "insulin antagonism" at the tissue level. With excessive caloric intake, the rates of fat and protein synthesis and of carbohydrate disposition are greatly enhanced, thus requiring an increase in the rate of insulin secretion. Indeed, in experimental animals, excessive ingestion of either calories or carbohydrate is associated with hyperplasia of the islets of Langerhans, an increase in circulating insulin levels, and alterations in the glucose and lipid metabolism of adipose cells (132), as well as their regulation by insulin. As previously discussed, these diet-induced changes parallel those observed in man. A potential role for such dietary factors in the altered metabolic state of the obese individual must, therefore, be considered. Some investigators have postulated that the abnormalities of carbohydrate and lipid metabolism, as well as hyperinsulinemia, develop during the course of obesity as a direct consequence of dietary factors; e.g., "insulin resistance" of obesity may represent an adaptive mechanism protecting the obese individual from a hypoglycemic reaction consequent to excessive caloric and/or carbohydrate intake (72).

4

Body Composition and the Natural History of Fatness

Gilbert B. Forbes

Human beings rank among the fattest of mammalian species. The newborn infant contains about 14 percent fat by weight. Young adult males have about 10-20 percent fat and females 15-30 percent fat, and most studies have shown that fat content continues to increase during the adult years. Pitts and Bullard found that most free-living mammals contain less than 10 percent fat (123). Data on measurements of skinfold thickness (some use the term "fat fold")--really the thickness of a double layer of skin and subcutaneous tissue--in large numbers of individuals both here and abroad suggest that relative fat content varies with age and sex (114, 149). Young infants tend to accumulate subcutaneous fat during the 1st year of life, peak values being attained at about age 1. At this time mean triceps skinfold thickness is 12 millimeters.

Afterward there is a gradual decline, to a mean value of about 10 millimeters in girls and 8 millimeters in boys at age 7; the formerly plump baby has now become a thin child. Throughout this period, which is prior to the maturation of secondary sex characteristics, girls tend to have thicker skinfolds than boys. Furthermore, the data of Owen et al. on total body water show that girl babies have a higher body fat content than boys (120). Hence the stage is set very early in life for the well-recognized sex difference in body fat content that characterizes the adolescent and the adult.

The increase in body fat content that accompanies the onset of puberty in both sexes is more pronounced in girls. Hence there is a tendency toward chubbiness in boys during the early years of puberty. Later on, the sex divergence becomes striking as the girl continues to put on fat while the boy tends to get thinner. By age 16, mean triceps skinfold thicknesses are 15 millimeters and 8 millimeters, respectively.

As noted above, the adult years are characterized by a gradual gain in fat and a fall in lean weight (29, 50), women remaining relatively fatter as the years go by.

The age changes in fat content and in lean body mass are of such a magnitude that comparisons between groups are not valid unless age is controlled, as well as sex. Furthermore, lean weight is related to stature, which means that height should be controlled as well (49).

Body composition analysis is required for estimation of adipocyte number, since the final answer is the product of the number of adipocytes per unit weight of fat and the total body fat content. Generally speaking, juvenile onset obesity is characterized by an increase in both size and total number of adipocytes (97), while adult-onset obesity is associated only with increased cell size (131). Body composition analyses also serve to characterize the nature of overweight, to distinguish those individuals whose apparent "excess weight" is due to a large lean body mass (LBM) from those who are truly obese.

Figure 1 shows data on the changes in triceps skinfold thickness that take place during infancy, childhood, and adolescence. Note the skewness that characterizes the frequency distributions of this body measurement and that is borne out by actual assays of total body fat (29).

Our data on LBM estimated by potassium-40 counting in a large series of normal subjects are illustrated in figure 2. In contrast to body fat content, LBM distributions for each age group tend to be symmetrical, the means and 50th percentiles being rather close. Note the sex difference in LBM that becomes manifest during adolescence, and that by late adolescence is so great that the average male LBM exceeds total body weight in the female.

It is against this background that body composition of obese individuals can be evaluated. In the first place, obese children tend to be a bit taller, to have a slightly advanced bone age, and to mature sexually at an earlier age than their nonobese peers. Recent data (51) show that children of normal weight who become obese during childhood often exhibit a concomitant acceleration in height, and further that

FIGURE 1.--50th and 90th percentiles for triceps skinfold thickness, based on data of Tanner and Whitehouse (149).

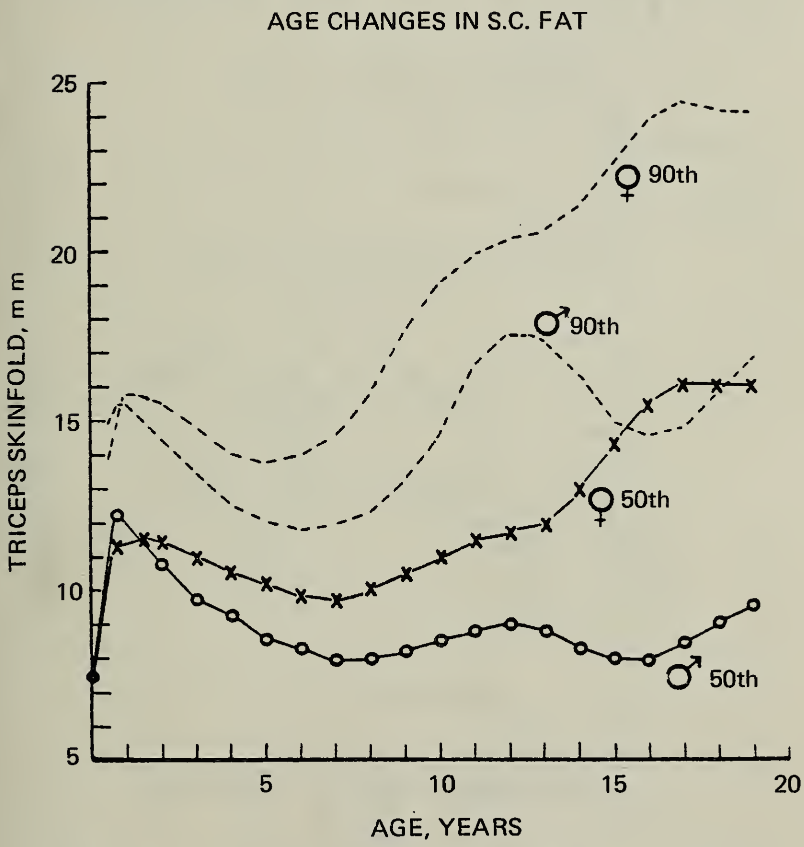

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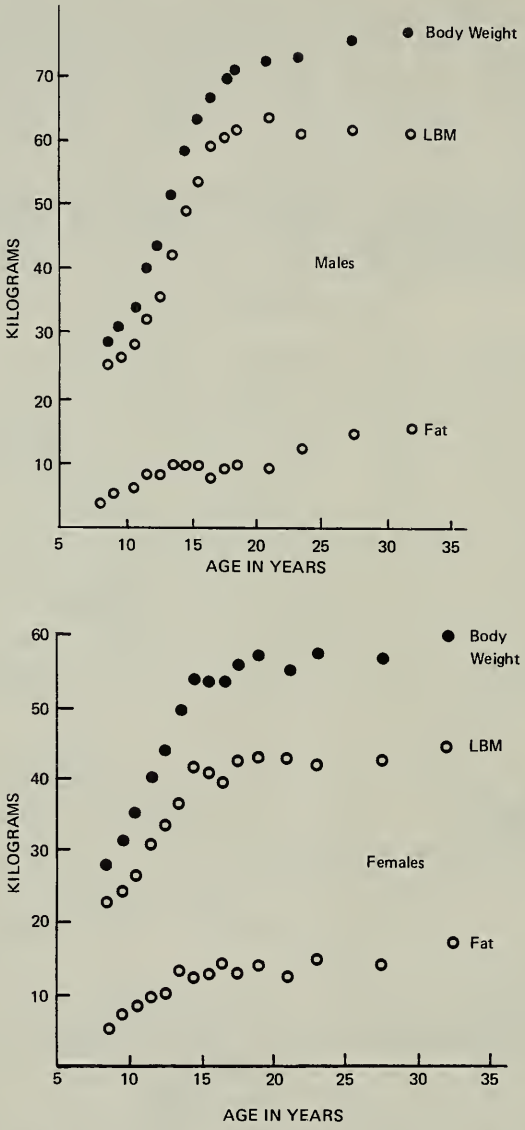
FIGURE 2.--LBM and total body weight, based on potassium-40 counting; 570 males and 450 females.



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the degree of relative height gain is proportional to the magnitude of the obesity (figure 3). Thus the overnutrition that generates the obese state accelerates growth, just as undernutrition acts to retard it.

Body composition studies show that obese individuals tend to have a somewhat larger LBM than nonobese individuals of the same height, age, and sex.

FIGURE 3.--Plot of relative height change as a function of relative weight change in children who became obese during childhood. The equation for the regression line is $y = 0.975 + 0.037x$.

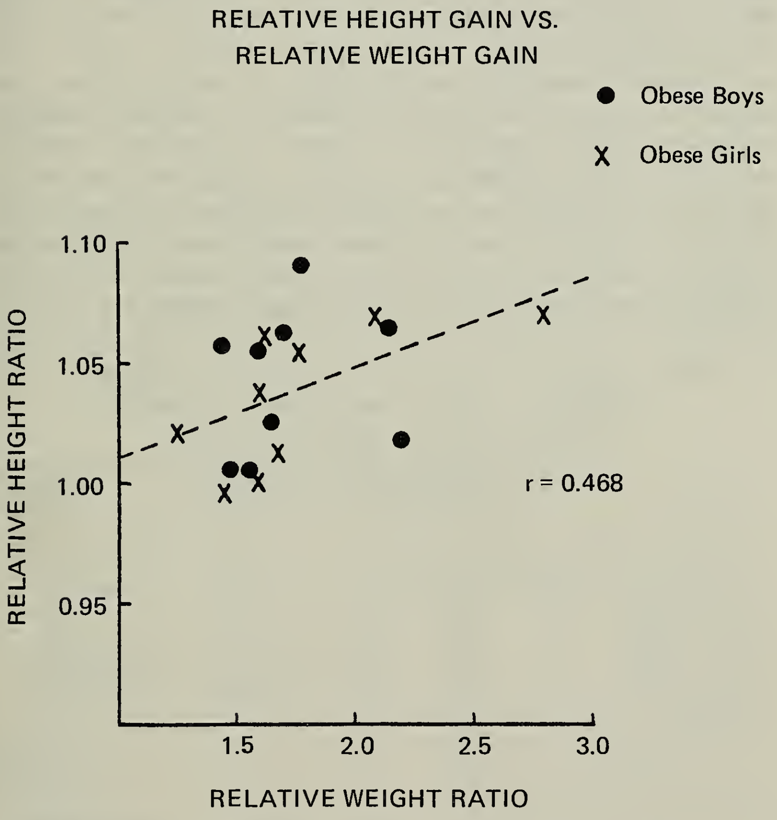

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Table 1 summarizes data from several studies of exogenous obesity. Though most of the excess weight is fat, some of it apparently can be accounted for by lean. As shown in the table, deliberate overfeeding of adult males leads to an increase in lean as well as fat; the increase in both these body components was proportional to the excess calories consumed. Nine subjects who consumed 32,000 excess calories during the experimental period gained an average of 4.4 kilograms in weight, of which 1.7 kilograms were lean; for the four who consumed 71,000 excess calories the average weight gain was 11.2 kilograms, of which 4.5 kilograms were lean (64). Rats nursed in small litters (155) or otherwise provided with an excess of milk from their mothers (80) also tend to put on more lean weight as well as fat.

These observations provide an explanation, at least in part, for the increase in adrenal steroid excretion manifested by obese individuals. More important, they give the lie to the frequent assertion that obese people do not eat the proper kind of food, for it is evident that the obese child must have eaten enough protein and other nutrient essentials to sustain his increased stature and greater lean weight.

TABLE 1.--Body composition in obesity

Subjects	N	Excess weight due to LBM (%)	Ratio obs/exp[a] LBM	Reference number
Boys and girls	27		1.09	(47)
14-yr-old boys	12	25		(121)
14-yr-old girls	9	32		(121)
Boys and girls	22		1.29	(32)
Adult women	17	30		(106)
Adult women	13		1.41	(105)
Adult men	8		1.18	(105)
Adult men	10	36		(27) deliberate overfeeding
Adult men	13	31		(64) deliberate overfeeding

[a] Expected LBM for age, sex, and stature.

Studies of certain types of experimental obesity tell quite a different story. Table 2 shows that rats subjected to hypothalamic lesions have a subnormal lean weight in the face of an excess of fat. One must conclude that such animal preparations do not provide a suitable model for human obesity.

There are large numbers of obese people in the United States. A few begin their careers in infancy [and indeed it can be shown that "chubby babies" are more likely to be obese as adults (31)], others start in childhood, and some wait until their adult years. We know that once established, childhood obesity tends to persist into adult life and that such individuals are most resistant to treatment. We also know that most obese children have one or more close relatives who are obese. Since established obesity is, in Mann's words, "an almost incurable disease" (108), the development of preventive measures should command a high priority. Possible, though as yet untried, measures include breast feeding, alterations in child-rearing practices, and promoting suitable energy-demanding activities to counteract the immobilizing influence of television and the automobile. Mothers should be discouraged from using food as a pacifier (28), athletic programs can be devised for the child who is chubby and a bit awkward, and the status of

TABLE 2.--Body composition in hypothalamic obesity (rat)[a]

Weight	Fat	LBM	Femur length	
	(g)	(g)	(g)	(cm)
Lesioned	391	179	212	2.8
Control	405	49	360	3.4
			Protein (g)	Body length (mm)
Lesioned	346	102	25	+22
Control	291	18	37	+58

[a]Data from references 63 and 75.

walking and cycling must be elevated in the eyes of the public.

It is likely that the stage for the development of obesity can be set in early life and that the relative hyperphagia that is responsible for it can be conditioned. The challenge to those seeking a means of prevention lies not in the hypothalamus, but rather in the hierarchy of brain centers that deal with the emotional phenomenon of appetite.

5

Obesity: Its Risks and Hazards

Alfred A. Rimm and Philip L. White

Previous reviews of the risks and hazards of obesity have methodically identified diseases or conditions found to appear more frequently in obese individuals. A number of studies, based mainly on the experience of insurance company clients, have also shown the extra mortality associated with slight, moderate, and marked overweight. These risks and hazards have been divided into three broad categories: 1) those associated with biochemical and physiological processes; 2) those associated with the psychosocial interactions in the environment of the obese individual; and 3) those associated with mortality among overweight individuals.

With the recent advances in the knowledge of underlying biological processes associated with obesity, it is now possible to develop hypotheses concerning the direct and indirect relationships between obesity and disease. This review, therefore, will attempt to synthesize current knowledge into a model depicting cause-and-effect relationships of the underlying biological processes and the clinical manifestations of diseases. In addition, a relatively primitive model will be proposed to help synthesize current knowledge concerning the effect of obesity on the psychosocial functioning of the obese individual.

Models are useful for describing complex biological states such as obesity, for which cause-and-effect factors may be hypothesized. What model best describes the underlying reasons for the simultaneous appearance of obesity and disease? Why do certain diseases appear more frequently among obese persons? Answers to these questions will be explained by presenting a "surface" model of obesity, which includes only observable clinical indicators (e.g., table 1), and a "deep" model of obesity, which includes

TABLE 1.--The parallel processes of obesity and prolonged cigarette smoking

	Vehicle	Behavior	Signs	Consequences
Smoking	Cigarettes	Prolonged smoking	Cough Shortness of breath Decreased taste Decreased smell sensitivity	Emphysema Cancer Duodenal ulcer Cirrhosis of liver Coronary artery disease Hypertensive heart
Obesity	Food	Prolonged excess food intake	Obesity (hypertrophy) (hyperplasia)	High blood pressure Resistance to insulin Gout Diabetes Arthritis Cancer Menstrual irregularities

the cause-and-effect processes at the biochemical and cellular level (e.g., figure 1).

For this review, we will define obesity as a chronic, almost incurable condition comprising an excess of fat tissue that is not the result of a frank genetic or hormonal disorder. Therapeutic measures for curing the obese individual have been for the most part disappointing; it seems that education and prevention are the only hopes for success. To be successful, prevention programs must show clearly that obesity is abnormal and dangerous. It is the raison d'etre for preventive programs.

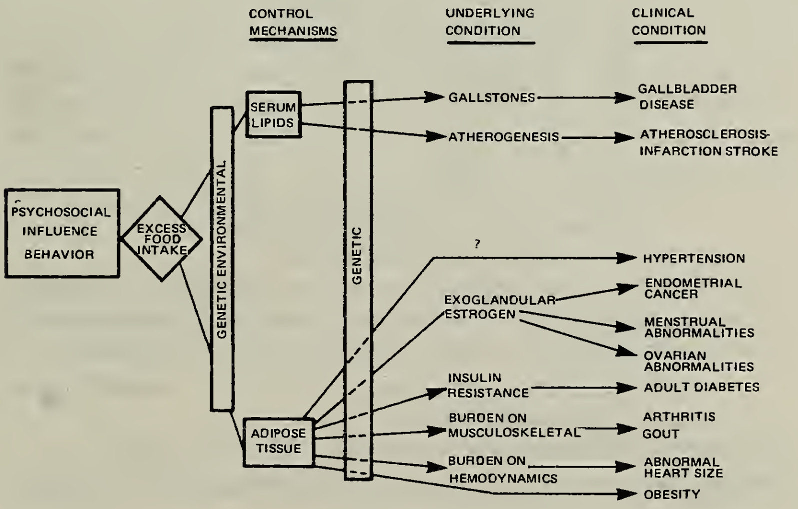
The hazardous aspects of obesity may be communicated by showing the parallelism between obesity and a well-known and well-documented habit such as prolonged cigarette smoking. Table 1 outlines the various signs associated with prolonged cigarette smoking and demonstrates that smoking modifies normal metabolic processes, resulting in signs of disease and its consequences. The model for obesity parallels the smoking model. In this surface model, obesity is considered a sign resulting from overeating relative to energy expenditure. The consequences of overeating include hypertension and other diseases. The analogy between obesity and smoking carries an important public health message that should help to dramatize the consequences of obesity.

Deep Obesity Model

A simplified deep model of obesity is presented in figure 1. It attempts to delineate the difference between obesity as a direct cause of disease and as a sign of a relative excess in food intake. The factors influencing excess food intake in our culture are not clearly understood.

Overeating may be defined as the degree of food intake that brings in more food energy than is expended. Unique genetic and environmental factors within each person affect how food is processed; for this reason, there are considerable differences between individuals. In figure 1, the vertical "genetic, environmental" box symbolizes a filter-like mechanism which governs how food is utilized. It has been well established that individuals given the same diets will have different lipid levels. Also accounted for in this box are differences in physical activity patterns affecting the pathways for food utilization. The second "genetic" vertical box depicts a "processor" mechanism that affects reactions at the biochemical

FIGURE 1.--Holistic, deep model of the processes associated with excess food intake.



level. Genetic differences are probably the primary reason why some persons with high serum lipids develop extensive atherogenic disease while others with the same levels do not. Exactly where and how this genetic "processor" operates to create variations between people is not clear. Simply stated, the two vertical boxes in figure 1 represent the unique internal food-processing machinery of an individual.

A classification scheme is necessary to help differentiate between cause and sign. The schema in table 2 is based on the metabolic changes that can be attributed to the adipocyte or the mass of adipose tissue. For obesity to promote or play a direct causal role in development of a disease, the mass of fat tissue must participate in triggering an abnormal condition. For example, the fact that fat cells as well as other cells are resistant to insulin, which interferes with

TABLE 2.--Classification of obesity as a cause of disease or a factor associated with disease

A. Causal. Diseases or conditions in which obesity is:

1. A primary contributing factor (causal association well documented)
    - a) Adult-onset diabetes
    - b) Menstrual abnormalities
    - c) Reproductive problems
    - d) Heart size and function
    - e) Arthritis
    - f) Gout
    - g) Hypertension

2. A secondary contributing factor
    - a) Endometrial carcinoma

B. Association. Disease or conditions which are correlated with obesity but not caused by obesity:

1. Atherosclerotic disease
2. Gallbladder disease
3. Death

glucose metabolism, demonstrates that these cells may have a direct role in modifying a normal metabolic process. In this situation, the hyperinsulinemia and resistance to insulin, with the accompanying low peripheral uptake of glucose, may result in adult-onset diabetes. Thus, obesity may be considered a primary contributing factor in diabetes.

A further example may help to distinguish between primary and secondary contributing factors. It has been suggested that the metabolism of certain steroid precursors in adipocytes plays a role in extraglandular estrogen production and that this role may be involved in endometrial cancer. In this instance, the fat tissue may be a contributing factor in the development of this tumor; since it is unlikely that elevated estrogen levels alone play a deciding role, it would be reasonable to consider obesity a secondary contributing factor in endometrial carcinoma. In contrast, extraglandular estrogen from adipose tissue may play a primary role in triggering the mechanism that leads to menstrual disturbances.

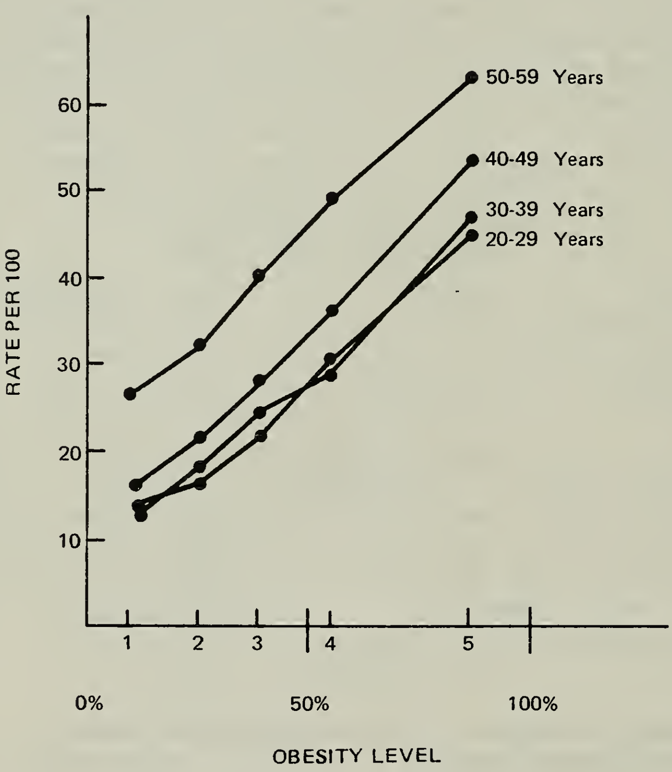
Because obesity operates as either a sign or a cause, it is possible to see why epidemiologic investigations may identify it as a risk factor for a disease when in fact it is only associated with the condition. For example, excess caloric intake may give rise to both obesity and elevated serum lipid levels. It is probably the elevated lipid levels that play a direct role in the formation of gallstones. In this example, both obesity and gallbladder disease may be traced back to the diet, and therefore they may be associated with each other. However, we would not say that obesity has a causal relationship with gallbladder disease; it coexists with this disease.

Evidence To Support the Deep Model and the Obesity Classification Scheme

Hypertension

A review of 39 different studies (33) concerned with the relationship between hypertension and obesity clearly indicates the existence of an association. The most dramatic relationship was observed in a study of women; figure 2 shows the strong linear relationship between the obesity level of women at different ages and a history of hypertension (127). It is noteworthy that the relationship between hypertension and obesity is similar for all age groups (that is, the curves are

FIGURE 2.--Obesity and age-specific occurrence rates for women with a history of high blood pressure.[a]

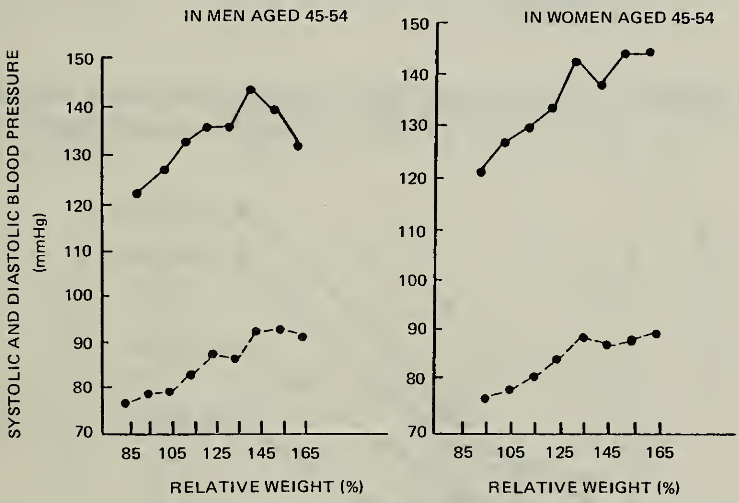


[From A. A. Rimm et al. Public Health Rep. 90:44-51, 1975.]

[a] Obesity level is expressed on a scale of percentage above ideal weight.

parallel). Figure 3 shows the average systolic and diastolic pressures relative to weight for both men and women, ages 45-54, from the Framingham Study (93); here the curves also show a linear association of blood pressure with obesity. The mechanism involved in elevating blood pressure among obese individuals has not been identified, as indicated by the question mark in the deep model (figure 1). Despite this uncertainty, obesity is classified as a cause of hypertension, because blood pressure decreases when excess weight is lost.

FIGURE 3.--Regression of systolic and diastolic blood pressure on relative weight. Framingham Study: exam 5.



Diabetes

Figure 4 depicts the relationship between obesity and insulin secretion. While the controlling mechanisms remain unclear, fat tissue apparently has two roles in promoting diabetes: it increases the demand for insulin, and it creates insulin resistance in obese individuals. Figure 5 shows the correlation between obesity and diabetes in a group of 73,532 women. For each age group, the prevalence of diabetes increases with increasing obesity. A more detailed analysis of women in the 40-59 age group was

FIGURE 4.--Model depicting interrelationship of obesity and adult-onset diabetes.

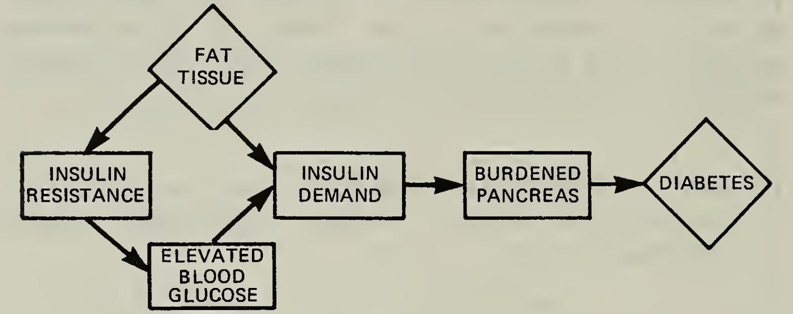
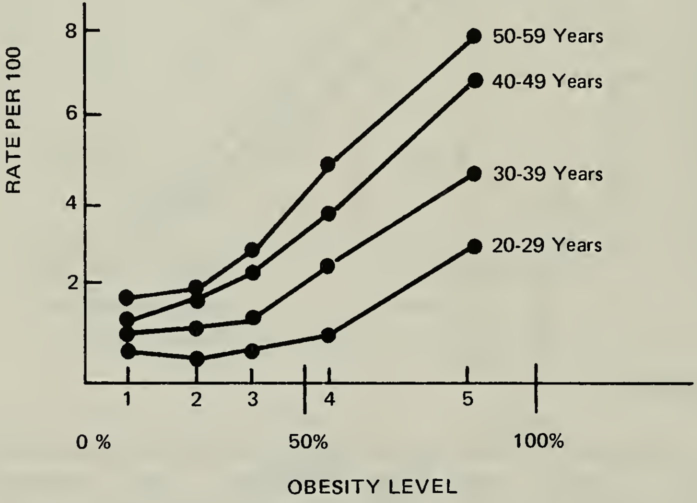


FIGURE 5.--Obesity and age-specific occurrence rates for women with a history of adult-onset diabetes.[a]



[From A. A. Rimm et al. Public Health Rep. 90:44-51, 1975.]

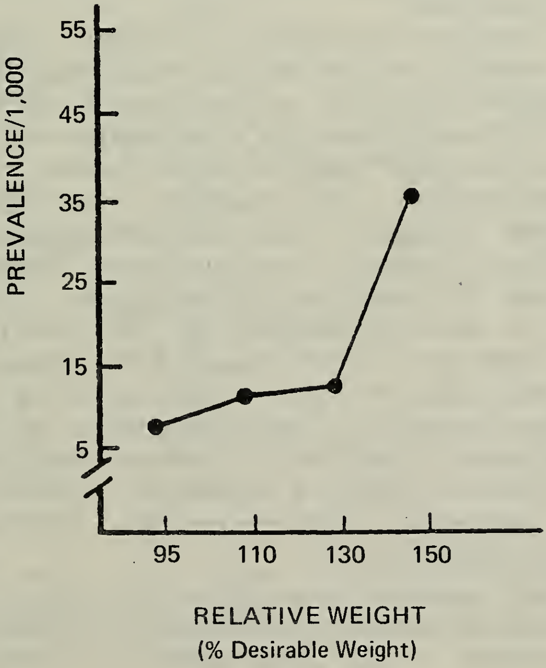
[a] Obesity level is expressed on a scale of percentage above ideal weight.

pursued to compare the risk associated with obesity to the risk associated with a family history of diabetes. The risk associated with obesity was twice as high.

Gout/Arthritis

It has been reported that weight loss often reduces the symptoms of bone and joint diseases, especially when the diseased bones and joints are weight bearing. A study of women showed the crude relative risk for arthritis to be 1.55, and that for gout, 2.56 (127). These results indicated that the occurrence of arthritis was 55 percent greater in the obese group (85 percent above the desirable weight) than in the group with the lowest weight (10 percent overweight), and that gout was 1.56 times more frequent in the obese group. Figure 6 gives the results from the

FIGURE 6.--Prevalence of gout by relative weight. Framingham Study: men (age-adjusted rates: 45-64).



Framingham Study, showing that as obesity in men increases (measured as relative weight) so does the prevalence of gout.

Abnormal Heart Size and Function

The size and weight of the heart are thought to increase with increasing body weight. Apparently, the burden of maintaining a greater mass in the obese individual results in myocardial hypertrophy. It is noteworthy that heart size and pumping return to near normal or normal following weight loss.

Menstrual and Ovarian Abnormalities

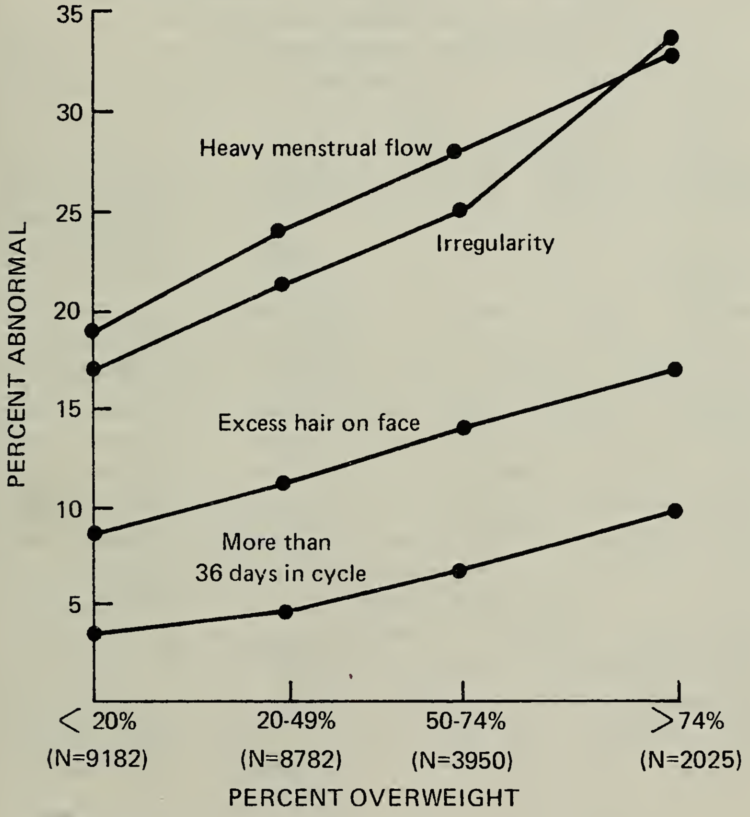
In a study of 36,081 women (78), obesity was found to be associated with heavy menstrual flow, irregular length of menstrual cycles, excess facial hair, and menstrual cycles greater than 36 days (figure 7). Other evidence supporting the association between obesity and ovarian function has shown that there are pathologic changes in the ovaries of women with morbid obesity (46).

One possible explanation for the association between obesity and menstrual disturbances is that some hormonal imbalance or hypothalamic abnormality underlies both conditions; the counterargument to this is that only in rare cases is obesity known to result from disturbances in hormonal secretion or hypothalamic damage. It has also been suggested that the emotional problems associated with obesity may play a role in menstrual abnormalities. There is evidence of some differences on the MMPI scales between obese and normal women and between those who are successful and unsuccessful at losing weight. Also, obese women are generally found to have a higher incidence of psychiatric problems than nonobese women. However, we do not know whether these specific psychologic differences are sufficient to affect menstrual function.

Another possible explanation is that obesity promotes anovulatory cycles and polycystic ovaries by causing estrogen to be either stored or synthesized.

Two hypotheses have been offered to explain how a disturbance in estrogen level results in polycystic ovaries: 1) if estrogen does not fall to levels compatible with the end of a normal menstrual cycle, follicle-stimulating hormone (FSH) is suppressed, preventing follicles from maturing sufficiently to produce a surge in estradiol and subsequently in the luteinizing hormone (LH), which triggers ovulation; 2) high estrogen levels sensitize the pituitary gland to GnRH, which increases LH in the serum, thus

FIGURE 7.--The relationship of weight to menstrual abnormalities.



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stimulating an overproduction of androstenedione and testosterone in the ovary. The increased production of testosterone may inhibit follicular maturation.

Endometrial Carcinoma

In a review (14) of 15 different investigations concerned with the relationship between obesity and endometrial carcinoma, some association was found in 14 of the studies (table 3). In a study of 56,000 women, an association was found between

TABLE 3.--Summary of studies of endometrial carcinoma. Definitions of obesity and authors' conclusions with respect to obesity in endometrial carcinoma

Author (year published)	Number		Mean age, cancer patients	Definition of obesity	Author's conclusion
	Cancer patients	Control			
Fox and Sen (1970)	300	300	--	Appearance	No association
Boutselis (1963)	269	--	60	Not given	64% endometrial cancer patients obese by modern medical standards
Corscaden (1947)	142	--	52	Increased weight of cancer patients	Obesity and cancer associated
Damon (1960)	438	291	56.8	Increased weight of cancer patients	Cancer patients significantly heavier than controls
Dunn et al. (1968)	55	114	63.6	Deviation from desirable	Cancer patients significantly more obese than controls
Garnet (1958)	50	50	--	> 160 lb	Cancer patients more obese
Javert and Renning (1963)	610	--	--	> 165 lb	24% of cancer patients obese
Kottmeier (1957)	617	--	--	> 180 lb	36% of cancer patients obese
Moss (1947)	23	--	61	> 10% above average weight	Cancer patients tend to be obese
Palmer et al. (1949)	772	--	57.5[a]	> 20 lb above average weight	53% of endometrial cancer patients obese
Peel (1956)	107	--	58	Appearance	Cancer patients may be more obese
Smith (1941)	307	--	--	> 160 lb	28% of cancer patients obese
Twombly and Jacobowitz (1962)	34	--	62	Increased weight of cancer patients	Cancer patients tend to be obese
Van Nagell et al. (1972)	75	75	62.1	> 20 lb above average weight	Obesity associated with cancer only in presence of diabetes
Wynder (1966)	112	200	55	Deviation from height-age-specific average weight	Obesity and cancer associated

[a] Median

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teenage-onset obesity and subsequent development of endometrial carcinoma; the results showed that women who had been obese as teenagers had 1.62 times greater risk of developing endometrial carcinoma compared with women who had not been obese as teenagers. This finding supports the hypothesis that prolonged estrogen stimulation, which may be associated with obesity, leads to cystic glandular hypoplasia of the endometrium, a condition that may precede endometrial cancer.

Atherosclerosis

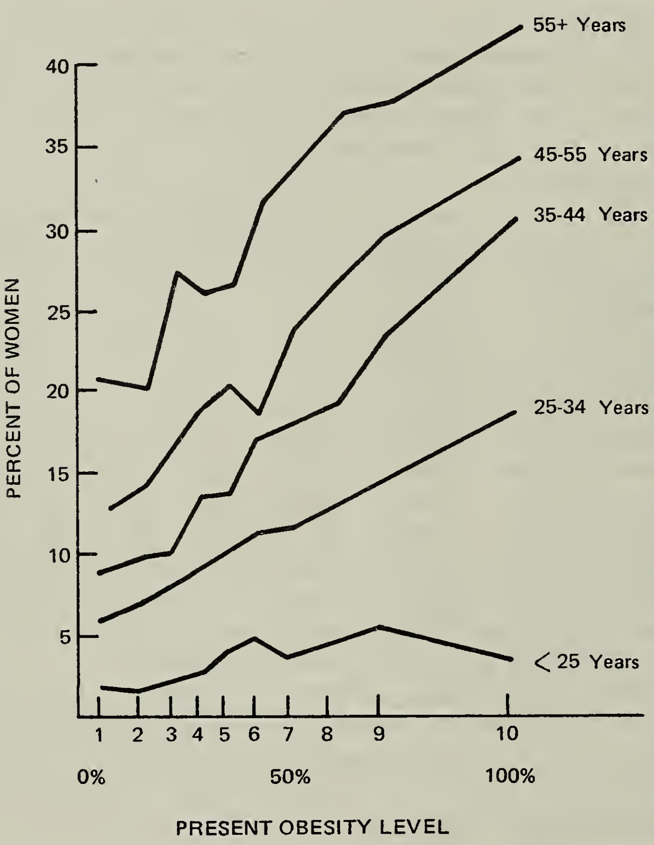
The Framingham Study gives the best available evaluation of the association between atherosclerotic diseases and obesity. Using the logistic function to evaluate factors associated with a 10-year incidence of cardiovascular disease, researchers found that the mortality rate was greater among persons with very high relative weight. Relative weight was also positively correlated with cardiovascular disease incidence in a study of both men and women; this association was found even after the researchers adjusted for other factors such as blood pressure, cholesterol, smoking, age, and diabetes. Furthermore, estimates from the Framingham Study indicate that coronary heart disease would decrease by 25 percent and congestive failure and brain infarction would decrease by 35 percent if everyone were at normal weight. These predictions are based on the assumption that the lifestyles and eating habits of our population cause obesity and that obesity is an ever-present sign that our habits and styles need changing.

The Build and Blood Pressure Study (137) demonstrates that even moderately overweight persons are subject to 50 percent more mortality from heart disease and about as much excess mortality from cerebral hemorrhage.

Gallbladder Disease

There is considerable evidence that gallbladder disease is associated with obesity. This association has been found at all age levels. Figure 8 shows that the prevalence of disease rises with increasing obesity and age; but even relatively young women, ages 25-34, show a strong positive correlation between degree of overweight and prevalence of gallbladder disease. Parity is also known to be a risk factor in women

FIGURE 8.--Percent with gallbladder disease history versus present obesity level for various age groups.[a]



[From A. A. Rimm et al. Public Health Rep. 90:44-51, 1975.]

[a] Obesity level is expressed on a scale of percent above desirable weight.

younger than 40. However, when adjustment is made for parity, obesity is still found to be highly correlated with gallbladder disease.

Mortality

There is ample evidence that obesity, or at least overweight, is associated with increasing mortality. A series of mortality/weight investigations of insured lives (6, 104, 137) has shown consistent results since the turn of the century. One study (137) found that the mortality rate increases with higher degrees of overweight and that this increase is more than proportionate to the departure from average weight. For example, men 20 percent above average weight showed about 25 percent more mortality; those 40 percent and 60 percent above average weight showed an increase in mortality of 67 percent and 150 percent, respectively. The rise in mortality among overweight women was distinctly lower. The mortality rate among overweight persons is increased significantly by the presence of other medical conditions. Optimum weights, that is, the weights associated with the lowest mortality rate, were generally 15-25 pounds below present average weights (see overview).

It is interesting, however, that in the Framingham Study relative weight was not found to be correlated linearly with mortality. Researchers in Denmark (138) studied a group of randomly selected young men between 1943 and 1973; they determined the mortality rate of the extremely overweight individuals to be 1.96/1000 man-years, whereas the expected rate was 1.23/1000 man-years. The primary causes of death among the extremely overweight men are given in table 4.

A Model for Psychosocial Aspects of Obesity

Table 5 gives a simple model summarizing some of the psychosocial factors associated with obesity which appear at different stages of life. It has been shown that an obese individual is considered "undesirable" by

TABLE 4.--Deaths in the group of extremely overweight young men

No.	Year of entry	Age of death	
1	1943	40	Pulmonary neoplasm
2	1947	36	Air crash
3	1949	52	Acute myocardial infarction
4	1949	33	Suicide
5	1950	37	Thrombosis of internal carotid, arteriosclerosis
6	1952	43	Suicide
7	1953	20	Pneumonia, acute appendicitis with peritonitis
8	1955	31	Myocardial insufficiency, hepatic cirrhosis
9	1955	18	Staphylococcal septicemia, neck abscess
10	1957	20	Traffic accident
11	1960	22	Traffic accident
12	1961	26	Pulmonary embolism, toe abscess
13	1962	26	Drowning
14	1964	22	Lightning
15	1964	27	Undetermined (died abroad)
16	1964	26	Acute myocardial infarction
17	1966	27	Traffic accident
18	1967	22	Acute pancreatitis
19	1973	19	Acute pancreatitis

TABLE 5.--Relation between obesity and psychosocial aspects of life

Stage of life			
Childhood	Adolescence	Young adult	Adult
Negative peer attitudes	Negative peer attitudes	Negative peer attitudes	Negative peer attitudes
Negative self-image	Negative self-image	Negative self-image	Job discrimination
	Underachievement in education	Job discrimination	Absenteeism

his or her peers. Some obese persons may have a disturbed body image; and, as they grow older, this disturbance may develop to include preoccupation with their own image, antagonism toward more obese individuals, and envy of thin persons.

Though obesity and intelligence are not correlated, performance in school has been found to be significantly higher among nonobese male students than among obese male students. Among young adults, there is evidence of discrimination against obese individuals. How often do we see an obese airline stewardess? In many occupations, attractiveness is a prerequisite. An obese individual may be prejudged as undisciplined, sloppy, and unreliable and thus may be discriminated against knowingly or unknowingly.

In the working environment, it has been shown that obese male blue-collar workers have poorer absenteeism records than do nonobese workers. This absenteeism is usually due to acute severe illnesses such as influenza. It has been hypothesized that obese workers are less able to cope with acute severe illnesses.

The most evident disabling psychologic features of obese persons result directly from their obesity. These features range from mild feelings of inferiority to very serious incapacities formed as a result of social stresses that interfere with normal socializing. Such stresses vary in severity, and it has been pointed out that their presence or absence depends upon the mores of the culture or subculture to which the obese person belongs.

It has been suggested that individuals with childhood-onset obesity have in some way become psychologically "imprinted" with obesity. When weight reduction produces a body size different from the "imprint," adverse psychological changes may occur. Such psychological changes have not been seen in patients with adult-onset obesity.

The well-known social attitudes toward obesity have been characterized as discrimination, stigmatization, and prejudice. It should be recognized that it is a generalization to assign a universal attitude to all ethnic and socioeconomic groups, but within the framework of contemporary America, the social stigma against an obese person is extant. This stigma has been described in four areas, each of which assigns different meaning to obesity: "1) in religion, as a sin;

2) in medicine, as a disease; 3) in crime, as a misdemeanor or felony, and 4) in aesthetics, as ugliness." It has also been pointed out that society's labels for obesity serve to create and accentuate the problems of being overweight: "The fat person's major handicap may not be his or her obesity, but the view that society takes of it" (5).

The prejudices and discrimination visited upon obese children include castigations by peers; academic, athletic, and social discrimination; and the probability of future business (job opportunity) discrimination. It has been pointed out that the greatest disadvantage of obesity in childhood is the likelihood of growing up to be an obese adult.

Summary Comments and Prospects for Action

The Senate Select Committee on Nutrition and Human Needs (152) has proposed dietary goals for the United States because, according to the introductory remarks, "...changes in our diet during this century are responsible for a wave of malnutrition, of both over- and underconsumption, that may be as profoundly damaging to the Nation's health as the widespread contagious diseases of the early part of the century." These changes in our diet, the committee notes, "...are linked directly to heart disease, cancer, obesity, and stroke, among other killer diseases...they are epidemic in our population."

The committee's report cites the following statement by Theodore Cooper, former U.S. Assistant Secretary for Health: "Obesity is considered a risk factor in cardiovascular disease, hypertension, atherosclerosis, hernia, gallbladder disease, diabetes mellitus, and liver disease...about 20 percent of all adults in the United States are overweight to a degree that may interfere with optimal health and longevity." The committee concluded from testimony at Senate hearings that " overconsumption of food in general has become a major public health problem."

The committee supports its conclusion concerning hazards from obesity with the statement "Reduction in obesity usually leads to reduction in serum lipid concentrations (reducing threat from heart disease), reduction in blood pressure (reducing threat of stroke), and improvement in glucose tolerance (reducing the threat of diabetes)...there is strong evidence suggesting that, for those overweight, the best protection against heart disease is weight reduction."

To emphasize the importance of overweight as a hazard, the second edition of the Dietary Goals for the United States began with a goal on overweight. The goal was stated as follows: "To avoid overweight, consume only as much energy (calories) as is expended; if overweight, decrease energy intake and increase energy expenditure" (151).

The recognition that obesity is a chronic condition that reduces the enjoyment of life and that it is associated with a higher incidence of degenerative disease provides the basis for accepting obesity as an important public health problem. The need to understand both the development and the treatment of obesity deserves high priority, as does the need to develop effective ways of applying current and developing knowledge.

Recommendations for Research

Our society has recognized obesity as a chronic condition with adverse effects, and its prevalence has been estimated to be greater than 40 million persons. How is it possible that such a widespread condition, which is a product of our environment, has not received more recognition in our health research priorities?

Diseases such as cancer, hemophilia, and end-stage renal disease have well-structured organizations that keep registries of persons with these diseases. These organizations maintain contact with the patient throughout his or her life. More recently, registries have been developed for patients receiving a particular therapeutic maneuver, such as kidney and bone marrow transplant and the aortocoronary bypass operation. The general purpose of registries is to maintain a pool of current information that can be used for studies evaluating factors associated with the natural history of the disease or the outcome following a therapeutic maneuver.

To study obesity and its etiology in our culture effectively, a National Obesity Registry (NOR) should be developed. This registry should be designed to follow obese individuals for a period of 30 years. In the very broadest sense, this registry should include three groups: 1) superobese children from all segments of society; 2) superobese adults from all segments of society; and 3) control groups, a cohort group for comparisons.

Some objectives of the NOR could include: 1) characterization of the natural history of obesity in our society; 2) long-term comparisons of psychosocial and behavior factors in obese and nonobese individuals; 3) evaluation of eating behavior and changes over time; 4) characterization of lifestyles of obese individuals; and 5) comparison of the "quality of life" between obese and nonobese persons.

The techniques for developing and maintaining registries are routine. The main problem in developing the NOR probably would be the identification of participants and their willingness to supply information to the registry.

An alternative to a national registry is a comprehensive long-term epidemiologic study of obesity in a single community, involving at least 3,000 obese subjects. This type of study could focus on the natural history of obesity and its relationship to other diseases; it could also evaluate familial patterns of obesity and investigate familial eating behavior as influenced by ethnic and socioeconomic status. A control group approximately one-half the size of the subject group would be necessary for appropriate comparisons.

Specific Research Needs

Even in an affluent society with a surfeit of food, most people maintain an even energy balance; why so many others escape this fine control is unclear. We need more information on exactly what regulates feeding. Water, glucose, fat and its metabolites, amino acids, and the thermic effect of food all have been implicated. It is not clear to what extent social factors can override these.

We do not know for certain if long-standing, early-onset, hyperplastic obesity perpetuates itself, nor do we understand the homeostatic mechanisms that maintain the heavier weight in persons with this form of obesity. Is this a consequence of a permanent hyperplasia of insulin-insensitive fat cells that promote appetite-stimulating hyperinsulinism? Is there a blunted ability to regulate intake to need? Are psychosocial factors involved?

In their efforts to evaluate the hazards and natural history of obesity, epidemiologic studies should take into account the individual's age at onset. More detailed population investigations of psychosocial and other determinants of obesity are also needed. Prospective studies should attempt to compare the cause, morbidity, and mortality associated with childhood-onset, hyperplastic obesity versus adult-onset, hypertrophic obesity.

The relative importance of nature and nurture in obesity needs to be better investigated. Parent-offspring and spouse aggregations need to be examined in more detail to determine the extent of genetic or environmental influence. Genetic linkage to the metabolic aberrations of obesity must be sought; specific biochemical lesions may exist in some familial obesity, and we must attempt to see through the dominant environmental factors to a possible underlying genetic component.

We also need to amass evidence on whether weight reduction actually improves health and cardiovascular prognosis in obese persons.

It is not clear whether there is some unique contribution of obesity to cardiovascular disease beyond its atherogenic effects. Is obesity specifically related to sudden death and congestive failure?

Evidence on whether being overweight affects survival once a cardiovascular attack occurs is sparse.

The reason for the negative association of obesity with intermittent claudication needs to be determined and confirmed.

Nor do we know the exact basis for the relationship between obesity and atherogenesis. To what extent are the excess calories eaten and to what extent is the content of the diet responsible for the hazardous consequences of obesity?

6

Physiological and Medical Concomitants of Obesity: The Framingham Study

W. B. Kannel and Tavia Gordon

Despite a general presumption that obesity is unhealthy and despite a large body of research into the physiology of adiposity, scientists have made little progress in unraveling its determinants, and its health consequences remain controversial. Some investigators depreciate its medical hazards despite extensive actuarial and epidemiologic evidence (96, 108). It is apparent that obesity and its health consequences are not completely understood. This report will focus on the physiological and medical associations of obesity as determined from long-term observations in the Framingham cohort.[1]

Methods

Researchers conducting the Framingham Study observed a group of 5,209 men and women, ages 30-59 in 1950, with repeated biennial examinations (66). These examinations included a standardized cardiovascular evaluation and a variety of blood chemistries, as well as a number of other tests and measurements. In addition, data on mortality and major cardiovascular

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NOTE: Portions of this paper, including tables 23-28 have been published previously [T. Gordon and W. B. Kannel, Obesity and cardiovascular disease: the Framingham Study. Clin. Endocrinol. Metab. 5(2):367-375 © 1976, W. B. Saunders Co. Further reproduction prohibited without permission of copyright holder.]

[1] A cohort is a representative closed population sample being followed longitudinally.

morbidity were obtained from a variety of sources, including death certificates and hospital records.

At each examination, the subjects were weighed on a clinical beam scale. Each subject wore an examination gown. Shoes and street dress were removed, but men wore their trousers. An extensive set of anthropological measurements, including several skinfolds and girths, was taken during the fourth and fifth biennial examinations but was not repeated on other occasions. Hence, the measure of obesity used in the study was weight relative to height, expressed as a percentage of a standard weight for height. The standard used in this article is derived from tables of desirable weight published by the Metropolitan Life Insurance Company. The reference table used is the following:

Height	Weight (pounds)		Height	Weight (pounds)	
(inches)	Men	Women	(inches)	Men	Women
55		94	65	131	128
56		97	66	135	132
57		100	67	140	136
58		103	68	144	140
59		106	69	148	
60	116	109	70	152	
61	119	112	71	157	
62	122	116	72	161	
63	125	120	73	166	
64	128	124	74	170	

While there are a variety of ways to translate measurements of height and weight into a measure of adiposity, they tend to be highly correlated. There is little reason to believe, as some do, that any is distinctly superior as an index of the percent of total body weight contained in adipose tissue. In any event, it is presumably not the quantity of fat tissue per se but the physiological consequences of gaining and maintaining excess adipose tissue that primarily interest us. Even a direct, precise measurement of body fat would itself be only an index of these physiological consequences.

Associations of relative weight with other characteristics are expressed in this report in the form of linear regression or product-moment correlations. This means that "obesity" is treated as a graded characteristic rather than as a discrete condition. Although we refer to "obesity" and "adiposity" in deference to convention, it should be understood that no sharp demarcations between obese and nonobese persons are intended. Moreover, grossly overweight people, who might have direct medical problems resulting from their massive body weight, were too few in this population to be examined separately. Details respecting specific measurements and disease criteria are published elsewhere (134). The number of persons taking selected examinations, by age and sex, is given in table 1. (All tables in this chapter appear together beginning on page 144.)

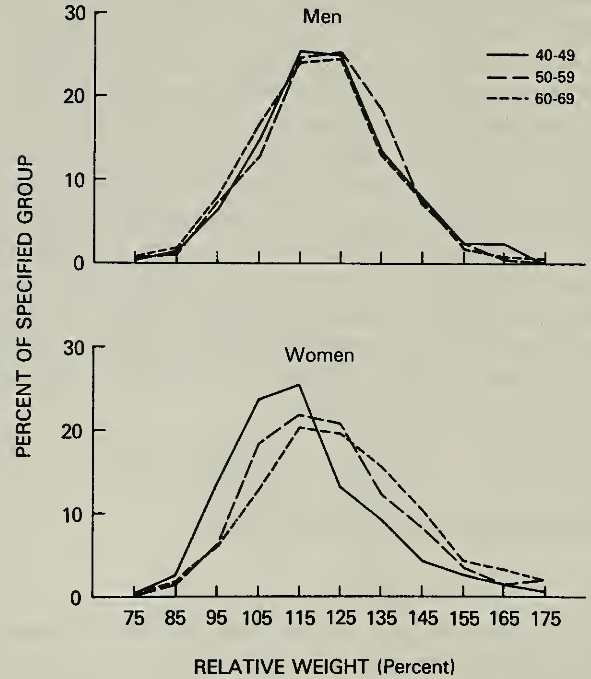
Means and Distribution of Relative Weight

Table 2 gives mean values and standard deviations of relative weight by age and sex at exam 1, when the study group was aged 29-62, and 18 years later at exam 10, when the group was aged 47-80. Figure 1 gives distributions for selected age groups.

It is obvious that the study group was, on the average, well above "desirable" weight and that only a small proportion of the cohort was below "desirable" weight. On the average, young women were closer to their desirable weight than any other age-sex group, but at exam 5 only 16.9 percent of women under age 45 were below the desirable weight for their height, while twice that number were 20 percent or more above it.

These findings are not unique to the Framingham cohort. Comparisons with data from a sample of the white population of the United States indicate that the Framingham population sample is very similar to the contemporaneous American population of the same age in both height and weight (128).

FIGURE 1.--Distribution of relative weight by age and sex. Framingham Study, exam 5.



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It is also evident that there are substantial secular differences; for example, men of a given age were more obese and women less obese at exam 10 than were persons of the same age at exam 1.

Cardiovascular Risks

Association with Lipids

At two points in the examination series extensive lipid testing was performed. One was at exam 2 when, by use of the analytical ultracentrifuge, serum lipoproteins were characterized in the range SF 0-400,[2] on casual specimens (8). The other occasion was during exams 10 and 11, when the surviving cohort was brought in fasting and plasma cholesterol levels were determined for the high-density, low-density, and very low-density lipoprotein (HDL, LDL, and VLDL) fractions separately, and total plasma triglyceride was measured. In addition, total serum cholesterol was measured on every examination, and serum phospholipid was characterized on exams 1-4 and exams 7-10. The correlation of relative weight with these lipids is given in tables 3 and 4.

There was considerable difference in the strength of the association between lipid levels and relative weight by age and sex. In general, relative weight was more closely related to blood lipid levels among men than among women of the same age. Furthermore, the strength of association was generally greater in younger persons than in older ones.

Obese persons tended in general to have higher lipid levels, with the distinct exception of HDL cholesterol, for which they generally showed lower levels. The strength of the relationship between this lipid and relative weight did not appear to vary by age or sex, at least within the age groups studied. This lipid was perhaps most strongly related of all the lipids to obesity. A closely correlated lipid, triglyceride (high triglyceride levels are associated with low HDL cholesterol levels), showed an almost equally strong relationship, obese persons having higher triglyceride levels. Since all these lipids are cardiovascular risk factors, it would appear likely that obesity is an important predisposing condition for cardiovascular disease.

Association with Blood Pressure

Figure 2 gives the regressions of systolic and diastolic blood pressure on relative weight for men

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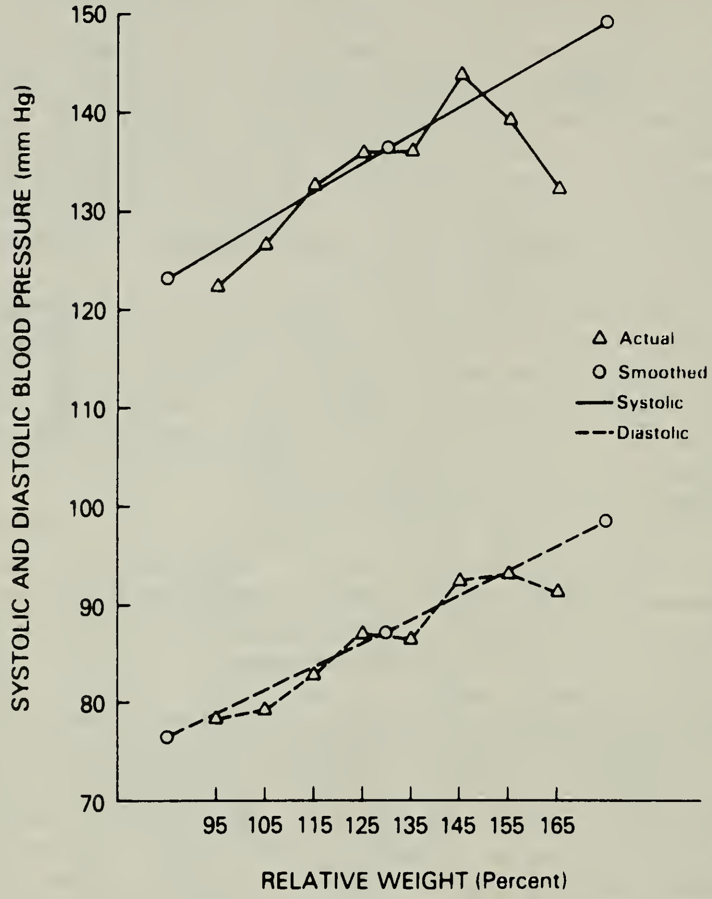
[2] SF = Svedberg ultracentrifuge flotation units.

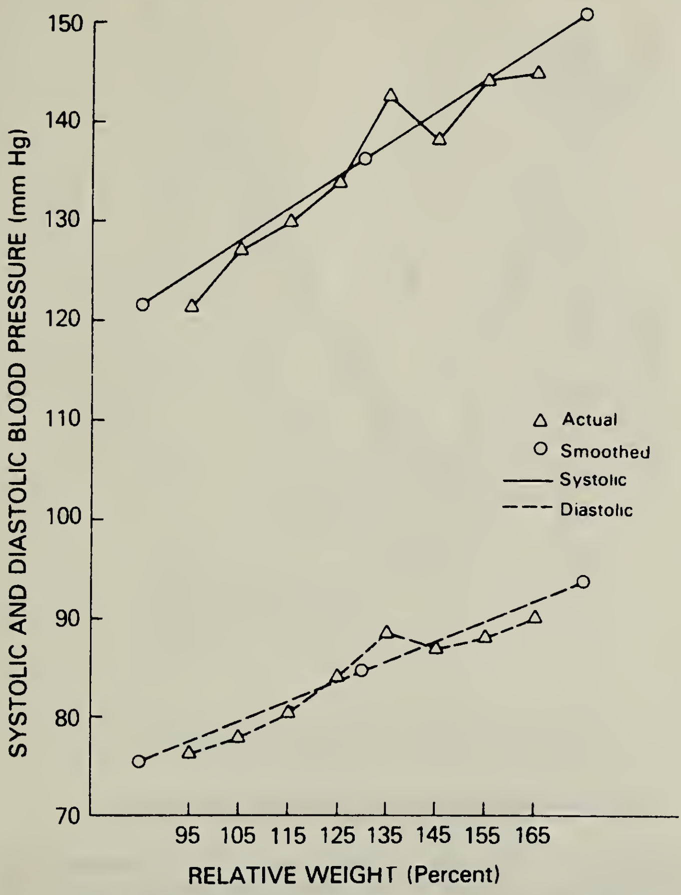
FIGURE 2.--Regression of systolic and diastolic blood pressures on relative weight in men ages 45-54. Framingham Study, exam 5.



ages 45-54. Figure 3 gives the regressions for women. Table 5 gives correlation coefficients by age and sex.

From these data it is evident that there was a moderately strong association between blood pressure and obesity, obese persons tending toward higher systolic and diastolic pressures, with only slight variations among age and sex groups. Diastolic pressures were somewhat more closely related to obesity than were systolic. Again, it is clear that

FIGURE 3.--Regression of systolic and diastolic blood pressure on relative weight in women ages 45-54. Framingham Study, exam 5.

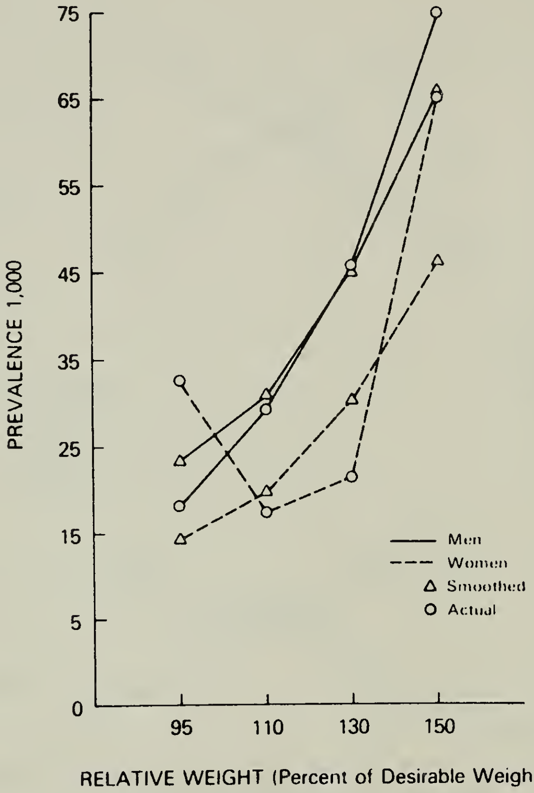


another major risk factor for cardiovascular disease is strongly influenced by relative weight. Since the sample regressions (figures 2 and 3) suggest a slight curvilinear component in addition to the linear regression, the actual associations may, in fact, be stronger than indicated in table 4.

Association with Glucose Intolerance

It is well recognized that increasing obesity is accompanied by an increasing blood glucose level, a greater likelihood of glycosuria, and an increasing

FIGURE 4.--Prevalence of glycosuria at exam 2 by relative weight. Framingham Study: men and women (age-adjusted rates: 45-64).



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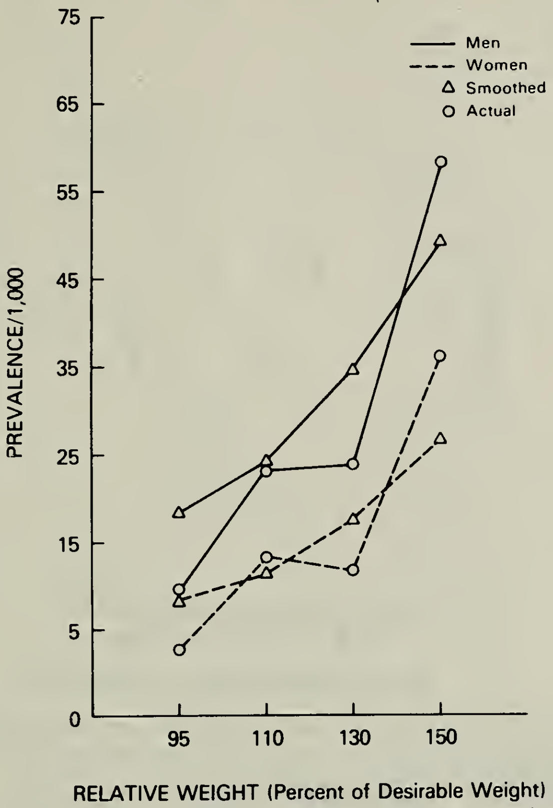
prevalence of diabetes. Tables 6-9 give data on the strength of these associations in the Framingham Study population. Figures 4 and 5 express the regression of glycosuria and diabetes prevalence as a function of relative weight. Because of the scanty number of cases, smoothed regressions are also included.

FIGURE 5.--Prevalence of diabetes at exam 2 by relative weight. Framingham Study: men and women (age-adjusted rates: 45-64).



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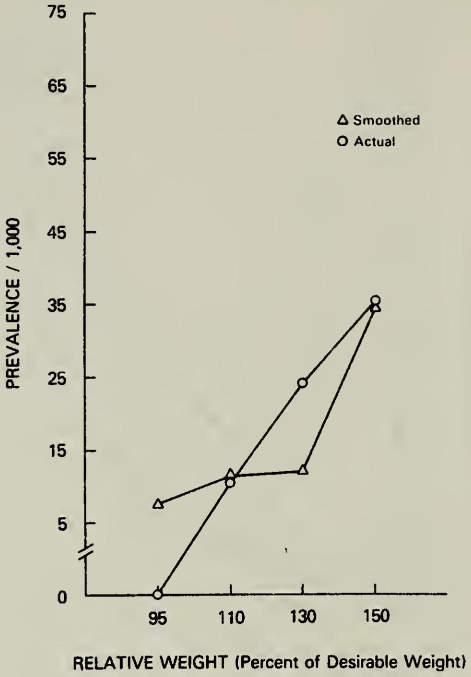
Blood glucose concentration was measured 1 hour after a 50-gram glucose load was administered to part of the study group at exam 10. It is of some interest that such measurements were more strongly correlated with obesity than were the casual measurements obtained on the remainder of the cohort (table 7). This presumably reflects the greater precision arising from standardized preparation.

FIGURE 6.--Prevalence of gout at exam 2 by relative weight. Framingham Study: men (age-adjusted rates: 45-64).



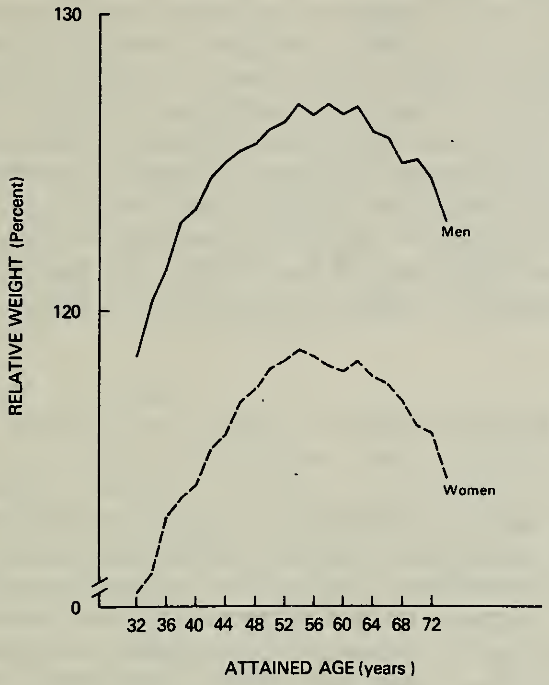
Association with Uric Acid and Gout

Tables 10 and 11 indicate the association of uric acid levels and gout with weight. Persons with hyperuricemia or gout tend to be obese, as is well recognized. By the same token, gout is more common in persons who are obese (figure 6).

Changes in Relative Weight

Individuals in the cohort tended to maintain their body weight throughout their adult life. Table 12 gives correlation coefficients for the first 10 exams. Body weight on the same persons correlated 0.956 after 2 years and 0.800 after 18 years. Table 13 indicates the

FIGURE 7.--Trends in relative weight with aging. Framingham Study: exams 1-10.



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extent of weight fluctuations. Large changes from one exam to another were relatively uncommon.

Nonetheless, there were noticeable changes in average relative weight as the cohort aged. These are summarized in figure 7, which gives an indication of the impact of age on weight in this cohort. Relative weight rose in both sexes to age 54, remained essentially unchanged until age 62, and then began to decline.

This trend, however, is based on a synthesis of the different cohorts in the Framingham Study population. If these cohorts were exhibited separately, they would show essentially the same slopes as those illustrated in figure 7, but the lines would not be joined because men born in later years tended to be heavier than men born earlier. However, the reverse was true for women in the cohort. This effect averaged roughly 6 pounds increase per decade for men and 3.5 pounds decrease per decade for women (table 14). Since later cohorts are taller than those born earlier (table 15), the change in relative weight--an increase of about 2 percentage points per decade--was slightly less marked for men. For women, changes in height worked in the other direction, leading to an average decrease of 5 percentage points in relative weight per decade.

Relation of Weight Change to Change in Characteristics

Regressions obtained on a single examination are, of course, based on one pair of measurements per person at one point in time. To measure the relation of actual change in weight to the change in some other characteristics, it is necessary to look at the data differently (8). This has been done for several characteristics (table 16). It is evident that increases in weight were, on the average, accompanied by increases in the levels of serum cholesterol, systolic blood pressure, and uric acid. While this was not equally evident for blood glucose, it is not unreasonable to suggest that a standard challenge before measurement might have led to a different result.

Other Measures of Obesity

Relative weight is the chief index of obesity used in the Framingham Study. It is well recognized that relative weight is not a precise measure of total body fat. Obviously, no indirect measure is; but some observers prefer to measure skinfolds, and others prefer body girths for an indirect assessment of total body fat.

Correlations among these measures are given in table 17. While the degree of these correlations varies by age, sex, and measure, it is obvious that they are all measuring generally the same thing.

However, to satisfy persons concerned with matters of this sort, we include three parallel tables of correlation coefficients using 1) relative weight, 2) subscapular skinfold, and 3) waist girth as the measure of obesity (tables 18-20). The differences are, as might be anticipated, of little consequence. In general, associations are slightly stronger with relative weight than with either subscapular skinfold or waist girth, presumably because weight is more precisely measured.

Sensitivity to Weight

Not everyone, of course, has an identical response to weight change. We may, therefore, ask whether those who develop cardiovascular disease are more likely to be sensitive to weight change, i.e., their blood pressure and serum cholesterol levels are more likely to rise and fall with changes in their weight.

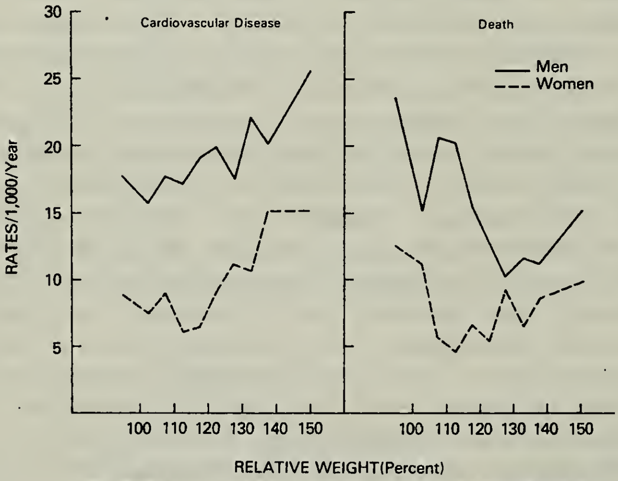
While in principle it is possible to examine this question directly, it is a good deal simpler, and more likely to be productive, to do so indirectly. To do this, we looked at the correlations between relative weight and serum cholesterol or blood pressure at exam 2 among those who in the next 16 years went on to develop cardiovascular disease, and among those who did not develop cardiovascular disease during followup.

For the risk variables presented in table 21, the correlations with obesity were generally stronger in persons who developed cardiovascular disease (other than intermittent claudication) during the next 16 years than in those who did not. The contrast was more noticeable in younger than in older persons and was greatest for uric acid and phospholipid. These findings are consistent with the notion that young persons whose atherogenic characteristics are especially sensitive to weight change may, as a consequence, be more vulnerable to subsequent cardiovascular disease.

Impact on Health

The relationship of relative weight to health, while well documented, is not well understood. There is a distinct excess over that expected in the incidence of cardiovascular disease and death in persons who are overweight. This excess death rate generally is higher when overweight is more pronounced (figure 8). To a considerable degree, this may be explained by the fact that blood pressure and serum cholesterol levels tend to rise as individuals gain weight, so persons who are obese have higher levels of blood pressure and serum cholesterol. There is also a positive association between relative weight and glucose intolerance and uric acid levels. Hence, we may argue that an increase in weight leads to an increase in other risk factors for cardiovascular disease.

FIGURE 8.--Two-year incidence of cardiovascular disease and death by relative weight. Framingham Study: 18-year followup.



NOTE: DATA SHOWN ARE CRUDE RATES FOR THE AGE GROUP 45-74

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However, this association of obesity with cardiovascular risk factors is less pronounced in women than in men. Yet obesity per se has at least as strong an association with the incidence of cardiovascular disease among women as it does among men.

Furthermore, the strength of relationship of obesity to disease incidence appears to decrease with age. At age 65-74, the association was not statistically significant for any cardiovascular endpoint (tables 22-26). In this respect, relative weight behaves more like serum cholesterol (or LDL cholesterol) than like blood pressure, for serum cholesterol as a risk factor is similarly age-dependent, whereas blood pressure is not. Another anomaly is the fact that intermittent claudication (table 23), also an atherosclerotic disease, was more likely to occur in lean than in obese persons. Framingham data leave little doubt that obese persons develop more cardiovascular disease than do lean persons (67). A comparison of obese [Metropolitan relative weight (MRW) $>$140] and lean persons($\leq$90 MRW) shows that the obese had a doubled incidence of brain infarction and congestive heart failure and a distinct but more moderate excess risk of coronary heart disease.

Since the cardiovascular sequelae are the most dangerous of all the consequences of obesity, they warrant a more detailed examination. Based on multivariate (adjusting for other major risk factors) regression analysis, it is apparent that the effect of obesity in promoting cardiovascular disease was greater in women than in men and that the effect diminished with advancing age (table 23). Comparing multivariate regression coefficients with bivariate ones (adjusting only for age) reveals that much of the effect of obesity is mediated through blood pressure and serum cholesterol levels.

With regard to specific cardiovascular diseases, obesity had the greatest impact on congestive heart failure (table 24) and brain infarction (table 25) among women; among men, its impact was roughly equivalent for all types of cardiovascular disease, except for a strong negative association with intermittent claudication (table 23). Significant net contributions of being overweight are found for men only for coronary heart disease (table 26) and for women only for congestive failure (table 24). With the evidence that low HDL cholesterol is associated with a significantly elevated risk of coronary heart disease and that it is more likely to be found in obese persons, we may reasonably anticipate that the net apparent impact of obesity even in men would be considerably reduced if total cholesterol were partitioned into its major components in the multivariate analysis. In more direct terms, obese and lean individuals with the same levels of blood pressure and HDL, LDL, and VLDL cholesterol probably have the same risk of cardiovascular disease. From a public health viewpoint, however, obese persons remain at greater cardiovascular risk precisely because they are more likely to have elevated blood pressure and LDL and VLDL cholesterol levels and depressed HDL cholesterol.

Compared with other risk factors, relative weight ranks quite low in men but somewhat higher in women, based on the size of the standardized regression coefficients for the various risk factors for cardiovascular disease and death (table 27). Nevertheless, because it reversibly promotes atherogenic traits like hypertension, diabetes, and hyperlipidemia, reduction of overweight is probably the most important hygienic measure (aside from the avoidance of cigarettes) available for the control of cardiovascular disease.

Estimation of Risk

A logistic function prepared for analytical purposes is different from one prepared for estimating risk. Before becoming medically concerned with a person's weight, it would seem sensible to estimate his or her risk of developing cardiovascular disease or of dying. Tables for assessing this risk are in print (110) but do not include relative weight as a risk factor. It may be helpful to supplement this information with a set of more complicated functions that include relative weight among the variables. These may be used to estimate the risk of persons ages 30-64 developing cardiovascular disease or dying within 10 years. The functions are restricted to persons initially free of cardiovascular disease (table 28).

The various second-order terms (age^2, age x cholesterol, age x cigarettes/day) are included to improve graduation and have no obvious analytic meaning; moreover, they confuse the analytical picture for age, serum cholesterol, and cigarette smoking. However, multiple logistic regression equations tabulated here may be of general use.

The negative coefficients for the regression of death on relative weight are somewhat puzzling, but they reflect a consistent finding in the Framingham Study: an increase in mortality at both low and high relative weights. This is not unique to the Framingham Study (40), but, despite considerable exploration of the data, we do not have a comprehensive explanation for this finding. It is partly accounted for by the fact that seriously ill persons who have lost weight because of their illness are at greater risk of death. The positive coefficients for cardiovascular disease are significant at a 5 percent level (on a one-sided test) so, even in the context of this large array of risk factors, relative weight makes a statistically significant contribution to the assessment of risk, although it may be less significant than the role played by weight-dependent factors like blood pressure, serum cholesterol, and diabetes.

Mechanisms

Little is known about how storage of calories in the adipose tissue raises lipids, elevates blood pressure, impairs glucose tolerance, and promotes hyperuricemia. The answer to this question should greatly enhance our understanding of the biology of obesity.

Obesity, like so many other chronic conditions, is more often controllable than curable and is more likely to respond to management if corrected early rather than late in its course. Also, like most chronic diseases, obesity is prone to exacerbations and recurrences.

The earlier in life obesity is established and the more pronounced it is, the more resistant it is to treatment (26). Based on existing evidence of the efficacy of treatment of long-standing pronounced obesity, it must be classed as one of the less tractable diseases. For this reason, it is better prevented than cured. It would be most helpful if the medical profession were to develop a sense of urgency about obesity, so when the disease is beginning or when it first appears, action would be taken immediately, as would be done for a lump in the breast or for high blood sugar. Only in this way can we avoid the refractory obese state. Once obesity is sustained for a long period, the evidence available suggests, it becomes a self-perpetuating condition as if homeostatic mechanisms have set a "thermostat" to maintain the heavier weight. Whether this is a consequence of permanent hyperplasia of insulin-insensitive fat cells, of blunted ability to regulate intake to need, or of psychosocial factors is unclear (108). Whatever the reason, it appears imprudent to allow obesity to develop fully and persist for any length of time.

Cardiovascular disease still accounts for half the annual toll of mortality in affluent countries, and chances of developing some major cardiovascular disease before age 60 are, for men, 1:3. There is every indication that this continuing epidemic has evolved from our way of life, and the remedy appears to entail altering our environment to one more favorable to cardiovascular health. Control of the surfeit of rich food intake and expansion of opportunities for exercise appear to be required, as do changes in our feeding practices that tend to use food as a form of entertainment rather than to sustain life.

For those who doubt that obesity poses a threat to cardiovascular health, only a clear demonstration that correction of long-standing obesity does in fact prolong life will suffice. In view of our poor performance in achieving sustained control of such obesity, this evidence will be a long time in coming. The question is: Can we afford iconoclasm while awaiting proof of efficacy? Not really, since weight control is logically the first approach to be tried in correcting or avoiding hypertension, diabetes, and hyperlipidemia.

There is no sound basis for predicting the benefit of a rigorous, controlled clinical trial, which at the present time seems manifestly impossible. It can be estimated from the Framingham data that if everyone were at optimal weight we would have 25 percent less coronary heart disease and 35 percent less congestive failure and brain infarctions. This potential benefit seems worth considerable effort to control or, better yet, to avoid obesity.

TABLE 1.--Number of persons by age and sex: Framingham Study, exams 1,2,5,9,10

Age at exam, by sex	Exam 1	Exam 2	Exam 5	Exam 9	Exam 10
Men					
29-34	392	170	0	0	0
35-39	443	449	89	0	0
40-44	422	359	423	1	0
45-49	357	371	362	236	81
50-54	374	323	353	386	370
55-59	279	302	285	301	309
60-64	69	157	259	289	291
65-69	0	1	170	222	223
70-74	0	0	2	171	172
75-79	0	0	0	41	95
Women					
29-34	458	197	0	0	0
35-39	584	531	111	0	0
40-44	511	510	507	2	0
45-49	451	429	469	293	104
50-54	432	425	436	478	460
55-59	372	376	396	409	427
60-64	65	192	337	342	355
65-69	0	0	217	322	318
70-74	0	0	5	259	242
75-79	0	0	0	81	146

NOTE: Includes all persons taking specified exams.

TABLE 2.--Mean relative weight by age and sex: Framingham Study, exams 1 and 10

Age at exam	Men Exam 1	Men Exam 10	Women Exam 1	Women Exam 10
	Mean relative weight			
29-34	117.3		110.8	
35-39	118.5		116.1	
40-44	118.8		118.2	
45-49	119.4	125.0	123.9	115.9
50-54	120.8	123.9	127.8	120.8
55-59	118.3	122.6	129.9	121.4
60-64	122.3	119.4	134.5	122.0
65-69		119.6		124.3
70-74		118.2		123.3
75-79		118.0		120.5
	Standard deviation			
29-34	16.67		18.99	
35-39	17.07		21.00	
40-44	16.23		20.93	
45-49	15.61	16.36	21.62	18.39
50-54	15.25	17.37	22.36	20.97
55-59	16.44	16.00	23.61	21.93
60-64	18.28	15.14	25.61	19.40
65-69		13.22		22.46
70-74		14.83		19.89
75-79		17.03		21.59

TABLE 3.--Correlation of relative weight with various serum lipids by age and sex: Framingham Study, exam 2

Age at exam 2, by sex	Total cholesterol	Phospholipid	Lipoproteins[a]			
			SF 0-12	SF 12-20	SF 20-100	SF 100-400
Men						
30-34	0.27	0.24	0.12	0.18	0.34	0.35
35-39	0.20	0.22	0.20	0.17	0.27	0.33
40-44	0.13	0.22	0.10	0.09	0.26	0.29
45-49	0.19	0.20	0.12	0.12	0.29	0.31
50-54	0.06	0.12	0.04	-0.02	0.15	0.23
55-59	0.06	0.14	-0.03	0.02	0.25	0.34
60-64	-0.01	0.10	0.08	0.04	0.27	0.37
Women						
30-34	0.08	0.09	0.08	0.13	0.29	0.26
35-39	0.10	0.08	0.11	0.10	0.23	0.24
40-44	0.05	0.15	0.08	0.09	0.30	0.32
45-49	0.07	-0.01	0.17	0.12	0.20	0.21
50-54	-0.03	0.01	0.08	0.01	0.08	0.07
55-59	-0.08	0.04	0.01	-0.05	0.10	0.17
60-64	-0.03	-0.03	-0.03	-0.01	0.09	0.15

[a] SF = Svedberg ultracentrifuge flotation units.

TABLE 4.--Correlation of relative weight with cholesterol fractions and fasting triglyceride by age and sex: Framingham Study, exam 10 or 11

	Cholesterol				
	Total	HDL	LDL	VLDL	Triglyceride
Men					
45-49	0.00	0.00	0.00	0.00	0.00
50-54	0.04	-0.16	0.13	0.01	0.21
55-59	0.06	-0.32	0.14	0.08	0.13
60-64	0.02	-0.21	0.03	0.09	0.01
65-69	-0.03	-0.27	0.10	-0.00	0.15
70-74	-0.11	-0.05	0.01	-0.12	0.05
75-79	-0.10	-0.29	0.23	-0.11	0.40
Women					
45-49	-0.10	-0.29	0.23	-0.11	0.40
50-54	-0.03	-0.29	0.06	0.06	0.15
55-59	-0.06	-0.19	0.14	-0.06	0.18
60-64	0.01	-0.27	0.08	0.09	0.17
65-69	-0.02	-0.28	0.08	0.02	0.19
70-74	0.02	-0.32	0.20	0.06	0.14
75-79	-0.09	-0.27	0.11	-0.07	0.22

TABLE 5.--Correlation of relative weight with systolic and diastolic blood pressure, by age and sex: Framingham Study, exams 1 and 10

Age at exam	Men		Women	
	Exam 1	Exam 10	Exam 1	Exam 10
Systolic blood pressure				
29-34	0.29	--	0.26	--
35-39	0.36	--	0.37	--
40-44	0.26	--	0.37	--
45-49	0.31	0.04	0.33	0.17
50-54	0.27	0.18	0.32	0.27
55-59	0.22	0.26	0.28	0.32
60-64	0.28	0.19	0.07	0.27
65-69	--	0.20	--	0.22
70-74	--	0.22	--	0.10
75-79	--	0.19	--	0.08
Diastolic blood pressure				
29-34	0.39	--	0.30	--
35-39	0.43	--	0.39	--
40-44	0.36	--	0.40	--
45-49	0.37	0.25	0.40	0.22
50-54	0.29	0.31	0.32	0.29
55-59	0.30	0.26	0.27	0.36
60-64	0.40	0.20	-0.02	0.34
65-69	--	0.30	--	0.26
70-74	--	0.18	--	0.09
75-79	--	0.26	--	0.19

TABLE 6.--Correlation of relative weight with blood glucose by age and sex: Framingham Study, exams 2 and 9

Age at exam	Men		Women	
	Exam 2	Exam 9	Exam 2	Exam 9
30-34	-0.08	--	-0.04	--
35-39	0.09	--	0.10	--
40-44	0.07	--	0.01	--
45-49	0.09	0.05	0.07	0.16
50-54	0.08	0.09	0.14	0.18
55-59	0.01	0.08	0.14	0.07
60-64	0.19	-0.01	0.02	0.20
65-69	--	0.09	--	0.02
70-74	--	0.12	--	-0.02
75-79	--	-0.04	--	0.10

TABLE 7.--Correlation of relative weight with blood glucose with and without glucose challenge: Framingham Study, exam 10

	Men	Women
Casual	0.02	0.11
With glucose challenge[a]	0.15	0.19

[a] 50 grams of glucose ingested one hour before specimen is taken.

TABLE 8.--Mean relative weight in persons with and without glycosuria by age and sex: Framingham Study, exams 2 and 10

	Exam 2 Glycosuria		Exam 10 Glycosuria		Number with glycosuria	
Age at exam	Present	Absent	Present	Absent	Exam 2	Exam 10
Men						
35-44	113.25	119.41	--	--	4	0
45-54	125.50	119.89	142.33	123.88	22	6
55-64	125.92	119.40	122.07	121.07	13	14
65-74	--	--	122.37	118.81	0	8
Age adjusted[a]	123.22	119.79	126.68	120.25	39	28
Women						
35-44	113.00	115.85	--	--	3	0
45-54	130.37	124.00	152.20	119.64	8	5
55-64	137.80	128.47	140.57	121.43	15	7
65-74	--	--	132.92	123.95	0	13
Age adjusted[a]	131.41	125.40	138.92	122.30	26	25

[a] Based on average weights for each 5-year age group weighted by the proportion of persons with glycosuria found in that age group.

TABLE 9.--Mean relative weight in persons with and without diabetes by age and sex: Framingham Study, exams 2 and 10

Age at exam	Exam 2 Diabetes		Exam 10 Diabetes		Number With Diabetes	
	Present	Absent	Present	Absent	Exam 2	Exam 10
Men						
35-44	121.56	119.27	--	--	9	0
45-54	125.36	119.87	133.62	123.54	25	26
55-64	128.15	119.11	123.03	120.72	20	64
65-74	--	--	122.37	118.55	0	40
Age adjusted[a]	125.29	119.47	124.65	119.98	54	130
Women						
35-44	112.00	115.78	--	--	6	0
45-54	129.80	123.92	140.05	119.13	15	22
55-64	139.62	128.23	129.21	121.02	26	53
65-74	--	--	132.18	122.80	0	60
Age adjusted[a]	132.69	124.62	130.92	121.32	47	135

[a] Based on average weights for each 5-year age group weighted by the proportion of persons with diabetes found in that age group.

TABLE 10.--Correlation of relative weight with uric acid levels by age and sex: Framingham Study, exam 2

Age at exam 2	Men	Women
35-39	0.37	0.34
40-44	0.32	0.34
45-49	0.33	0.12
50-54	0.20	0.31
55-59	0.37	0.29
60-64	0.25	0.19

TABLE 11.--Mean relative weight in persons with and without gout by age and sex: Framingham Study, exams 2 and 10

Age at exam	Exam 2 Gout Present	Exam 2 Gout Absent	Exam 10 Gout Present	Exam 10 Gout Absent	Number with gout Exam 2	Number with gout Exam 10
Men						
35-44	141.00	119.21	--	--	3	0
45-54	132.60	119.88	136.83	123.78	10	12
55-64	126.44	119.37	124.25	120.83	9	24
65-74	--	--	123.48	118.68	0	21
Age adjusted[a]	132.25	119.49	126.22	120.53	22	57
Women						
35-44	--	--	--	--	0	0
45-54	150.00	123.99	147.00	119.85	1	2
55-64	154.50	128.66	131.00	121.52	2	5
65-74	--	--	127.00	123.78	0	4
Age adjusted[a]	153.00	127.29	132.00	121.88	3	11

[a] Based on average weights for each 5-year age group weighted by the proportion of persons with gout found in that age group.

TABLE 12.--Correlation in the Framingham Study of body weight between two exams, by sex, for subjects taking exam 10 and specified exam

Number of years later	Examination 1	2	3	4	5	6	7	8	9
Men									
0	1.000								
2	0.956	0.963	0.959	0.958	0.957	0.953	0.957	0.954	0.952
4	0.944	0.944	0.937	0.941	0.933	0.938	0.935	0.926	
6	0.925	0.923	0.917	0.919	0.919	0.919	0.909		
8	0.907	0.908	0.892	0.904	0.897	0.892			
10	0.892	0.885	0.880	0.884	0.873				
12	0.864	0.869	0.860	0.858					
14	0.850	0.853	0.833						
16	0.828	0.822							
18	0.800								
Women									
0	1.000								
2	0.951	0.947	0.953	0.958	0.961	0.958	0.954	0.948	0.948
4	0.917	0.928	0.934	0.939	0.940	0.936	0.931	0.918	
6	0.901	0.916	0.917	0.921	0.919	0.911	0.907		
8	0.888	0.900	0.897	0.901	0.894	0.886			
10	0.876	0.881	0.881	0.879	0.868				
12	0.856	0.863	0.856	0.854					
14	0.838	0.833	0.822						
16	0.807	0.801							
18	0.774								

TABLE 13.--Number of persons according to the difference between the highest and the lowest value of body weight measured at the specified exams by sex: Framingham Study, exams 1 to 10

Highest minus lowest value	Persons with weights known at exams specified								
	1 and 2	1-3	1-4	1-5	1-6	1-7	1-8	1-9	1-10
Men									
0	124	10	1	0	0	0	0	0	0
1-4	978	477	194	96	42	25	6	3	2
5-9	664	758	673	514	374	264	194	138	99
10-14	225	396	496	525	496	448	389	321	257
15-19	94	163	258	302	338	350	337	333	300
20-24	22	60	100	136	197	219	239	248	253
25-29	13	24	50	77	95	120	143	140	138
30-34	2	7	20	40	45	70	77	93	96
35-39	3	5	10	18	23	24	42	44	48
40 or more	2	4	10	15	22	40	54	69	84
Average individual variation									
Range	5.6	8.6	11.2	13.3	15.0	16.9	18.5	19.9	21.2
Standard deviation	4.97	5.09	5.47	5.77	6.02	6.36	6.66	6.87	7.09
Women									
0	165	17	1	0	0	0	0	0	0
1-4	1,219	580	272	140	64	25	14	7	5
5-9	785	887	804	629	513	401	298	205	157
10-14	269	480	566	637	591	562	515	438	355
15-19	132	212	315	362	413	437	416	419	384
20-24	37	100	140	184	228	239	278	301	305
25-29	12	35	68	87	106	126	140	155	161
30-34	11	24	36	63	72	86	105	110	124
35-39	4	11	23	28	37	57	67	74	82
40 or more	7	21	31	36	46	62	77	97	117
Average individual variation									
Range	5.8	9.3	11.9	13.7	15.3	16.8	18.3	19.8	21.2
Standard deviation	5.16	5.53	5.80	5.96	6.12	6.32	6.53	6.77	7.04

TABLE 14.--Estimates of cohort changes in weight and relative weight

	Exam		Body weight		(Second-First)	Relative weight		
	First	Second	First	Second	Difference	First	Second	Difference
Men								
40-44	1	6	167.8	176.4	8.6	118.8	122.1	3.3
45-49	1	6	166.7	173.5	6.8	119.4	121.5	2.1
50-54	1	6	168.7	171.5	2.8	120.8	120.7	-0.1
55-59	1	6	162.3	169.0	6.7	118.3	120.7	2.4
60-64	3	8	162.0	168.6	6.6	118.3	121.1	2.8
65-69	5	10	161.9	166.0	4.1	119.0	119.6	0.6
Average					5.9			1.9
Women								
40-44	1	6	138.5	137.5	-1.0	118.2	115.4	-2.8
45-49	1	6	144.6	141.1	-3.5	123.9	119.4	-4.5
50-54	1	6	148.7	140.3	-8.4	127.8	119.4	-8.4
55-59	1	6	149.5	143.9	-5.6	129.9	123.0	-6.9
60-64	3	8	147.2	144.5	-2.7	128.0	124.0	-4.0
65-69	5	10	144.5	144.7	+0.2	126.3	124.3	-2.0
Average					-3.5			-4.8

[a] Relative to Metropolitan Life Insurance Company tables.

TABLE 15.--Mean height by age and sex for persons measured on exams 1 and 10, Framingham Study

	Mean height (inches)		Number
Age at exam 1	Exam 1	Exam 10	of persons
Men			
29-34	68.43	68.10	245
35-39	68.00	67.47	288
40-44	67.84	67.18	225
45-49	67.34	66.69	181
50-54	67.10	66.34	143
55-59	66.59	65.79	108
60-62	66.56	65.63	12
Women			
29-34	63.02	62.94	291
35-39	62.74	62.49	345
40-44	62.68	62.27	303
45-49	62.34	61.69	218
50-54	62.19	61.51	211
55-59	61.83	60.93	150
60-62	62.04	60.84	26

TABLE 16.--Regression of changes in various characteristics on changes in Framingham relative weight: Framingham Study, 16-year followup

Characteristic	Number of persons	Regression coefficient Value	Regression coefficient Standard error	% of variance
Men				
Serum cholesterol (mg/100ml)[a]	1,216	1.13	0.065	3.9
Systolic blood pressure (mmHg)[b]	1,492	0.66	0.038	4.6
Blood glucose (mg/100ml)[c]	943	0.25	0.062	1.1
Uric acid (mg/100ml)[d]	1,650	0.033	0.0033	3.5
Women				
Serum cholesterol (mg/100ml)[a]	1,286	0.63	0.055	2.0
Systolic blood pressure (mmHg)[b]	1,939	0.45	0.032	2.7
Blood glucose (mg/100ml)[c]	1,088	0.13	0.041	-0.1
Uric acid (mg/100ml)[d]	1,791	0.017	0.0021	1.7

[a] Exams 2-9.
[b] Exams 3-9.
[c] Exams 2-4, 6, 8.
[d] Exams 2-4.

NOTE: The regression coefficient b is given for the equation $y = a + bx$, where y is the change in the characteristic, x is the change in Framingham relative weight. See Ashley and Kannel (8).

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TABLE 17.--Correlation of relative weight with some other measures of obesity by age and sex: Framingham Study, exam 5

Age at exam 5, by sex	Number of persons	Body weight	Waist girth	Skinfolds	
				Flank	Scapula
Men					
35-39	89	0.891	0.914	0.775	0.791
40-44	423	0.911	0.911	0.736	0.730
45-49	362	0.888	0.742	0.698	0.660
50-54	353	0.895	0.868	0.669	0.742
55-59	285	0.879	0.864	0.591	0.672
60-64	259	0.905	0.863	0.697	0.695
65-69	172	0.915	0.877	0.677	0.686
Women					
35-39	111	0.965	0.804	0.596	0.650
40-44	507	0.972	0.906	0.680	0.722
45-49	469	0.979	0.912	0.654	0.741
50-54	436	0.973	0.885	0.596	0.696
55-59	396	0.976	0.889	0.632	0.689
60-64	337	0.975	0.908	0.568	0.666
65-69	222	0.975	0.915	0.653	0.736

NOTE: Relative weight based on Framingham median weights for height.

TABLE 18.--Correlation of various characteristics with relative weight by age and sex: Framingham Study, exam 4

Age at exam 5, by sex	Number of persons[a]	Serum cholesterol	Blood pressure Systolic	Blood pressure Diastolic	Blood glucose	Uric acid
Men						
35-39	252	0.16	0.23	0.33	-0.09	0.32
40-44	423	0.17	0.31	0.34	0.06	0.33
45-49	347	0.22	0.25	0.30	0.09	0.34
50-54	349	0.07	0.25	0.31	0.16	0.21
55-59	288	-0.02	0.21	0.27	0.01	0.34
60-64	259	-0.02	0.18	0.20	-0.02	0.30
65-69	91	0.09	0.22	0.19	0.10	0.44
Women						
35-39	297	0.19	0.28	0.33	0.09	0.33
40-44	531	0.13	0.42	0.43	0.04	0.35
45-49	466	0.09	0.26	0.36	0.03	0.25
50-54	407	0.01	0.35	0.38	0.11	0.24
55-59	387	-0.01	0.35	0.41	0.11	0.30
60-64	334	0.11	0.29	0.29	0.09	0.33
65-69	110	-0.11	0.23	0.18	-0.05	0.19

[a] Total taking exam 4.

TABLE 19.--Correlation of various characteristics with waist girth by age and sex: Framingham Study, exam 4

Age at exam 5, by sex	Number of persons	Serum cholesterol	Blood pressure		Blood glucose	Uric acid
			Systolic	Diastolic		
Men						
35-39	252	0.14	0.23	0.29	-0.11	0.32
40-44	423	0.17	0.32	0.32	0.06	0.30
45-49	347	0.19	0.27	0.32	0.10	0.38
50-54	349	0.01	0.26	0.33	0.18	0.17
55-59	288	-0.04	0.17	0.21	0.00	0.26
60-64	259	-0.01	0.17	0.22	0.03	0.27
65-69	91	0.09	0.13	0.14	0.11	0.49
Women						
35-39	297	0.11	0.24	0.26	0.04	0.31
40-44	531	0.09	0.35	0.36	0.01	0.25
45-49	466	0.05	0.21	0.32	0.05	0.27
50-54	407	-0.01	0.24	0.28	0.08	0.24
55-59	387	0.00	0.29	0.35	0.14	0.29
60-64	334	0.05	0.19	0.19	0.07	0.32
65-69	110	-0.07	0.14	0.19	-0.14	0.20

TABLE 20.--Correlation of various characteristics with subscapular skinfold by age and sex: Framingham Study, exam 4

Age at exam 5, by sex	Number of persons	Serum cholesterol	Blood pressure		Blood glucose	Uric acid
			Systolic	Diastolic		
Men						
35-39	252	0.07	0.08	0.17	-0.08	0.22
40-44	423	0.13	0.25	0.26	0.05	0.27
45-49	347	0.12	0.14	0.20	0.23	0.23
50-54	349	0.04	0.20	0.20	0.19	0.07
55-59	288	-0.10	0.16	0.18	0.07	0.22
60-64	259	0.00	0.11	0.07	0.17	0.27
65-69	91	0.04	0.33	0.27	0.16	0.34
Women						
35-39	297	0.08	0.19	0.18	0.05	0.34
40-44	531	0.17	0.34	0.38	0.08	0.31
45-49	466	0.06	0.17	0.21	-0.06	0.17
50-54	407	0.12	0.19	0.22	0.05	0.24
55-59	387	0.03	0.33	0.30	0.27	0.19
60-64	334	0.08	0.14	0.10	0.18	0.23
65-69	110	-0.07	0.29	0.26	-0.06	0.31

TABLE 21.--Correlation of relative weight with some other characteristics at exam 2 according to subsequent cardiovascular experience. Framingham Study: persons free of cardiovascular disease at exam 2

Sex, characteristic	Less than 45		45-54 years		55 years and over	
	CVD[a]	No CVD	CVD[a]	No CVD	CVD[a]	No CVD
Men						
Serum cholesterol	0.173	0.184	0.170	0.131	0.029	-0.045
Systolic blood pressure	0.328	0.272	0.287	0.249	0.020	0.253
Diastolic blood pressure	0.446	0.394	0.299	0.293	0.150	0.299
Uric acid	0.513	0.301	0.317	0.284	0.250	0.294
Phospholipid	0.210	0.197	0.263	0.181	0.069	0.077
Women						
Serum cholesterol	0.219	0.113	0.014	0.056	-0.077	-0.044
Systolic blood pressure	0.216	0.299	0.116	0.321	0.330	0.196
Diastolic blood pressure	0.341	0.342	0.215	0.341	0.256	0.176
Uric acid	0.404	0.278	0.300	0.279	0.237	0.107
Phospholipid	0.476	0.164	0.247	0.060	0.151	0.050
Number of persons[b]						
Men	93	795	172	438	125	225
Women	47	1,041	102	644	131	342

[a] Coronary heart disease, congestive heart failure, stroke.

[b] Total free of CVD at exam 2, by age at exam 2.

TABLE 22.--Regression of 2-year incidence of cardiovascular disease on relative weight: Framingham Study, 18-year followup

Age	Regression coefficient		T-value	
	Men	Women	Men	Women
45-54	0.0109	0.0175	2.29	4.29
55-64	0.0072	0.0099	1.65	3.21
65-74	0.0037	-0.0001	0.53	-0.02
Average, all ages	0.0072	0.0098	2.73	4.51
Bivariate[a]	0.008	0.0092	2.76	4.14
Multivariate[b]	0.004	0.0028	1.32	1.14

NOTE: Logistic regression estimated by method of Walker-Duncan.

[a] Adjusted only for age.
[b] Adjusted for other major risk factors.

TABLE 23.--Regression of 2-year incidence of intermittent claudication on relative weight, 18-year followup Framingham cohort, men and women 45-74

Age	Regression coefficient		T-value	
	Men	Women	Men	Women
45-54	-0.0197	0.0243	-1.51	2.59
55-64	-0.0118	0.0011	-1.27	0.13
65-74	-0.0217	-0.0039	-1.54	-0.40
Average, all ages	-0.0161	0.0072	-2.41	1.35
Bivariate[a]	-0.0158	0.0047	-2.38	0.84
Multivariate[b]	-0.0193	-0.0016	-2.79	-0.28

NOTE: Logistic regression estimated by method of Walker-Duncan.

[a] Adjusted only for age.
[b] Adjusted for other major risk factors.

TABLE 24.--Regression of 2-year incidence of congestive heart failure on relative weight: Framingham Study, 18-year followup

Age	Regression coefficient		T-value	
	Men	Women	Men	Women
45-54	0.0165	0.0129	1.50	1.17
55-64	0.0061	0.0235	0.61	4.93
65-74	0.0161	0.0087	1.31	1.24
Average, all ages	0.0122	0.0182	1.93	4.89
Bivariate[a]	0.0124	0.0177	1.95	4.64
Multivariate[b]	0.0057	0.0111	0.85	2.72

NOTE: Logistic regression estimated by method of Walker-Duncan.

[a] Adjusted only for age.
[b] Adjusted for other major risk factors.

TABLE 25.--Regression of 2-year incidence of brain infarction on relative weight: Framingham Study, 18-year followup

Age	Regression coefficient		T-value	
	Men	Women	Men	Women
45-54	0.0056	0.0312	0.32	3.87
55-64	0.0223	0.0171	1.73	2.41
65-74	-0.0069	0.0106	-0.41	1.26
Average, all ages	0.0100	0.0196	1.14	4.36
Bivariate[a]	0.0100	0.0184	1.13	3.94
Multivariate[b]	0.0031	0.0089	0.35	1.76

NOTE: Logistic regression estimated by method of Walker-Duncan.

[a] Adjusted only for age.
[b] Adjusted for other major risk factors.

TABLE 26.--Regression of 2-year incidence of coronary heart disease on relative weight: Framingham Study, 18-year followup

Age	Regression coefficient		T-value	
	Men	Women	Men	Women
45-54	0.0144	0.0178	2.73	3.78
55-64	0.0109	0.0109	2.31	3.16
65-74	0.0089	-0.0022	1.10	-0.40
Average, all ages	0.0119	0.0101	3.68	4.09
Bivariate[a]	0.0119	0.0094	3.70	3.72
Multivariate[b]	0.0101	0.0024	2.98	0.84

NOTE: Logistic regression estimated by method of Walker-Duncan.

[a] Adjusted only for age.
[b] Adjusted for other major risk factors.

TABLE 27.--Average univariate standardized logistic regression coefficients for death and cardiovascular disease incidence: Framingham Study, 18-year followup

Independent variable	Cardiovascular disease		Death	
	Men	Women	Men	Women
Relative weight	0.125	0.216	-0.189	-0.060
Serum cholesterol	0.230	0.270	-0.099	-0.017
Systolic blood pressure	0.419	0.470	0.294	0.254
Diastolic blood pressure	0.342	0.378	0.195	0.172
Vital capacity	-0.173	-0.332	-0.384	-0.411
Diabetes	0.169	0.202	0.116	0.218
LVH-ECG	0.223	0.252	0.361	0.294
Cigarettes/day	0.223	0.038	0.226	0.130

NOTE: Logistic regressions were calculated for each 10-year age group in the range 45-74 and weighted by the inverse of their variances to compute average coefficients. Estimated by method of Walker-Duncan.

TABLE 28.--Logistic regression coefficients for the 10-year incidence of cardiovascular disease and death given certain characteristics in persons free of cardiovascular disease at exam 2, Framingham Study

Characteristics	Cardiovascular disease		Death	
	Men	Women	Men	Women
Relative weight (percent)	0.0094358[b]	0.0075781[b]	-0.0082315	-0.0007280
Age (years)	0.4230619[c]	0.1260685[c]	0.1612311	-0.0116870
Diastolic blood pressure (mmHg)	0.0204239[c]	0.0153156[b]	0.0264676	0.0159573
Serum cholesterol (mg/ml)	0.0205275[b]	0.0145005	0.0025045	0.0104825
Cigarettes/day	0.0599176[b]	0.0497954	0.0723086	0.0689721
Vital capacity (dl)	-0.0013572	-0.0032197[b]	-0.0052825	-0.0020435
Pulse rate	0.0065277	-0.0004253	0.0140600	-0.0048993
Diabetes[a]	1.2064293[c]	1.5525138[c]	1.0304984	1.4785188
LVH-ECG[a]	1.3089251[c]	1.1578399[b]	0.9611221	1.3074035
Age^2 (age x age)	-0.0028447[b]	0.0001755[b]	-0.0006176	0.0013050
Age x cholesterol	-0.0002344	-0.0002030	-0.0000071	-0.0001837
Age x cigarettes/day	-0.0005473	-0.0005620	-0.0007502	-0.0008564
Constant	-21.1296685	-12.1306775	-10.5036815	-6.7035243

[a] Present (definite) = 1, not present = 0

[b] /t/ ≥ 1.65.

[c] /t/ ≥ 2.33.

7

Conservative Approaches to Treatment

Theodore B. Van Itallie

Control of Energy Intake

Fasting

Elaborate studies on the alterations of fuel homeostasis during starvation have demonstrated that fasting can be well tolerated by obese humans even for prolonged periods of time, the most obvious limitation being the loss of body protein during starvation and the resulting implications for vital body functions. In general, prolonged starvation as a therapeutic procedure has met with only a few difficulties, although a variety of possible side effects and an occasional death have been observed during therapeutic starvation of obese patients.

Researchers have frequently noted a transitory rise of serum transaminases during prolonged starvation without understanding its mechanism or significance. In addition, fasting is associated with the occurrence of hyperuricemia, and the development of arthritis and renal uric acid calculi has been reported in obese subjects during starvation.

The most frequent early side effects during total starvation are hypotensive episodes and, later, transient phases of fluid retention. Management of both these complications rarely causes any significant problems. A few instances of severe complications due to cardiovascular disturbances have been described during prolonged therapeutic starvation. Electrolyte imbalances, vitamin deficiencies, emotional disturbances, neutropenia, and ketoacidosis have also occurred. In fact, the literature contains reports of a few deaths in obese patients on starvation regimens.

Because of such complications, all patients should be hospitalized during prolonged starvation to ensure that sufficient amounts of fluids, electrolytes, and vitamins are given and that bodily functions are closely monitored. When these precautions are adhered to, significant side effects, except for occasional orthostatic hypotension, are rare.

Therefore, in the hands of the experienced physician, starvation need not be considered an adventurous approach to the treatment of obesity. Nevertheless, it is not recommended as a routine therapeutic procedure, mainly for two reasons. 1) Excessive loss of lean tissue occurs early in starvation. After several weeks, these losses greatly diminish. Thus, neither short-term periods of fasting (less than 2 weeks) nor intermittent fasts are of particular benefit. 2) Total fasting in the hospital is expensive, and the long-term results may not justify the cost since most patients regain weight.

Adherence to fasting is generally good because patients must agree in advance to starvation therapy; thus, less than 5 percent drop out before 3 weeks of treatment have been completed. However, the long-term results are rather poor. After 2 years, not more than one-third of the patients have maintained their lowered body weight; this outcome is independent of age, sex, degree of original overweight, age of onset of obesity, or apparent physical activity level. But these poor results can be improved upon by close and continuing followup, including dietary instruction and behavioral therapy. After an appropriate period of total starvation, the patient should be introduced to a program of long-term conventional therapy.

In summary, the treatment of obesity by prolonged total starvation, if it is to be undertaken at all, should be restricted to the few selected patients with severe obesity in whom a rapid weight loss appears to be vital and from whom long-term cooperation can be anticipated.

Supplemented Fasting

Cure or even long-term control of massive obesity is seldom achieved, but the morbidity, complications, and lethal potential of this condition are well recognized and justify efforts aimed at palliation. From the public health standpoint, a primary outpatient approach to therapy is dictated by the multitude of patients and the long duration of treatment. "Supplemented fasting" represents such an approach; it exploits the energy deficit of fasting and its high degree of patient adherence while simultaneously modifying ketosis, hyperuricemia, hypoglycemia, and clinical side effects so as to permit safe usage outside the hospital. Three groups have now reported using this technique, employing lean beef (1.1-1.4 grams per kilogram of desired weight) or 30-45 grams of egg albumin combined with 20-30 grams of carbohydrate per day. Suitable quantities of vitamins and minerals are provided. Frequent clinic visits serve to reinforce adherence and to permit monitoring of clinical and biochemical effects.

In one program, approximately 1,200 patients were treated with the supplemented fasting method. Seventy-eight percent of the patients lost more than 40 pounds, with losses proportional to initial body weights. When the initial body weight was 235 pounds for women and 300 pounds for men, weight loss averaged 85 pounds at a weekly rate of 3.0 pounds for women and 4.5 pounds for men. Similar rates of weight loss have been reported by other groups employing similar regimens. Hypertension ameliorated in 90 percent and disappeared in 67 percent of patients who were not on antihypertensive drugs, and hypertensive medication could usually be withdrawn from those on prior treatment. Previously untreated diabetics or those on low-dose insulin or sulfonylurea treatment became normoglycemic and aglycosuric, often within 1 to 3 weeks, but almost always by 3 months. Diabetics on 50 or more units of insulin daily improved more slowly and might still require some insulin. Other clinical benefits included relief of dyspnea; improved mobility; facilitation of needed abdominal, pelvic, and orthopedic surgery and of coronary angiography followed by coronary revascularization procedures; relief of infertility; and, finally, improvement in self-esteem, family relationships, and occupational status.

Side effects, similar to but more tolerable than those involved in total fasting, included fatigue, orthostatic dizziness, hair loss, skin dryness, cold intolerance, muscle cramps, amenorrhea, and decreased libido. In rare instances, lithium intoxication, peroneal nerve palsy, and postrealimentation cholecystitis or pancreatitis was encountered. A few sudden deaths occurred in patients with prior evidence of heart disease. While the immediate cause of death appeared to have been ventricular arrhythmia, the nature of the underlying cardiac pathology remained unclear. Biochemical abnormalities were minimal, consisting of a small decline in hematocrit; occasional persistence of serum uric acid concentrations higher than 10 milligram percent, requiring allopurinol or probenecid; and transient elevation of SGOT and SGPT soon after the start of the regimen.

Extending this technique to the larger problem of weight maintenance following weight reduction has shown more limited advantages in preliminary experience. Reuse of supplemented fasting after major weight regain is successful in only 25 percent of patients, compared with 78 percent on a first attempt. One week of supplemented fasting at 4- to 8-week intervals has been used to augment dietary regimens, as has individual and group work with the physician in a maintenance clinic. In a 6- to 15-month followup of 110 patients, 30 percent were within 10 percent of the weight recorded when supplemented fasting was terminated. In contrast, 5 percent of the patients had regained 90 percent of the lost weight. Between these extremes of success and failure are the majority of patients with varying degrees of maintenance. The relatively small number of followup patients points up one of the critical problems in obesity management: despite exhortations, positive reinforcement, telephone contacts, and previous histories of weight regain, only 30 percent of the patients attend a maintenance clinic with any sort of regularity. The rest drop out because of an unrealistic feeling of mastery over their problems or because of discouragement, embarrassment, or guilt at even a minor regain of weight. We can hope that the addition of behavior modification and lifestyle techniques to maintenance programs will allow significant inroads to be made in the problem of long-term control of obesity. In the meantime, supplemented fasting provides a valuable means for prompt alleviation of morbid obesity and improvement of accompanying hypertension, diabetes, and other associated conditions, placing the patient in a more advantageous position from which to strive for control of caloric intake.

The widely marketed very-low-calorie "protein diet"[1] is based on the use of liquid protein products and includes powdered protein, to be mixed with liquid, and protein capsules and tablets. The availability of these products has made possible their use by many people, often without medical supervision.

In theory, consumption of protein alone induces the body to burn fat and spares muscle tissue, minerals, and other materials that constitute the lean body mass. Consumption of such products in the recommended amounts with no supplementation furnishes 300-500 calories per day, an amount that nutritionists consider insufficient for maintenance of good health.

By the end of 1977, the Food and Drug Administration had received reports of more than 40 deaths associated with very-low-calorie protein diets. The Center for Disease Control found that in at least 15 of these deaths the diet was highly suspect as a contributing factor. All the victims were obese women, ages 25-51, who had lost an average of 83 pounds after 2-8 months on the diet. None had a history of heart disease. All died suddenly of heart irregularities, either while on the diet or shortly after discontinuing it.

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[1] Material on the "protein diet" excerpted from N. Glick, Low-calorie protein diets, FDA Consumer, March 1978, pp. 7-9.

In addition, more than 100 people reported to the FDA that they had become ill while using these products. Their symptoms included nausea, vomiting, diarrhea, constipation, faintness, muscle cramps, weakness or fatigue, irritability, intolerance to cold weather, decreased sex drive, hair loss, and skin dryness. More serious medical problems included dehydration, gout recurrence, and hypokalemia.

A panel convened by the FDA in October 1977 concluded that these products should not be taken without supervision by medical personnel trained in their use. The panel recommended that the products not be used by persons taking prescription drugs; those with kidney, liver, or heart disease or high blood pressure; by the elderly; by preschool children or adolescents; or by pregnant women or nursing mothers.

The FDA now requires that a warning label be placed on all protein supplements intended for use in weight reduction or maintenance programs.

Low-Calorie Diets

Low-calorie diets seem best considered in relation to two broad questions: how do they work, and what are their physiologic effects.

The first question must be viewed in the light of rapidly accumulating information about the many ways humans interact with food. Such information indicates that, in addition to caloric and nutritional considerations, one must also take into account nonnutritional factors such as palatability, variety, individual conditioned responses to food, and the presence of food-related cues in the environment. These factors often play an important, even a decisive, role in an individual's eating behavior.

Weight reduction diets can be divided into two types of regimens: those that overtly restrict calories, and those that do not actually specify calorie reduction but instead manipulate the diet or the circumstances of eating to induce a spontaneous decrease in energy intake. Low-calorie diets can be "balanced," providing a more-or-less conventional distribution of fat, carbohydrate, and protein; or they can be "unbalanced," for example, the low-carbohydrate ketogenic diets and very-low-calorie protein diets.

Regimens that do not specify calorie reduction but are designed to decrease spontaneous energy intake may utilize any of a number of approaches. Some may work by greatly narrowing food choices, e.g., carbohydrate restriction, or by limiting intake to nutritionally complete food homogenates, in either liquid or solid form. Such regimens appear to reduce or eliminate the incentive to overeat provided by the usual array of conventional foods. Indeed, the further a regimen is removed in appearance, taste, and consistency from regular food, the less likely it is to sustain the positive feedback response to eating that makes it so difficult for most obese persons to adhere to a diet of palatable, low-calorie meals. This fact may explain why some obese patients can readily hold to a diet that tastes--and is taken--like medicine, but are unable to follow a low-calorie regimen that merely restricts intake of normal foods. Diets that greatly narrow food choices, restrict all carbohydrates, or limit all intake to a liquid homogenate also are easier to follow because they obviate the need to count calories.

Other approaches that have been proposed for weight control include a diet of fiber-rich foods (dietary fiber being thought to serve as an effective obstacle to overeating) and the substitution of various calorically reduced analogs of energy-rich foods like margarine, dietetic mayonnaise, and low-calorie soft drinks. Theoretically, nonabsorbed or poorly absorbed food analogs also could be used to reduce the calorie density of the diet.

Because fat, carbohydrate, and protein are not fully interchangeable as fuel sources, the physiologic response to calorie restriction is affected by the composition of the diet as well as by its energy content. Of particular importance is the fact that diets low in both calories and carbohydrates are ketogenic (unless the protein moiety provides a sufficient excess of glucogenic amino acids). Some observers believe that ketosis acts to suppress hunger, thereby making adherence to a ketogenic diet easier. However, other workers in the field have been unable to document an anorexic effect of nutritional ketosis, so the issue remains unresolved. During the first few weeks of treatment with a hypocaloric, low-carbohydrate diet, the rate of weight loss is especially rapid because patients exhibit a water diuresis and become somewhat dehydrated. A similar dehydrating effect is also induced by hypocaloric protein diets.

Low-carbohydrate diets do not spare body protein more effectively than do isocaloric, balanced diets. The ability of a given low-calorie diet to spare protein seems to depend on a number of factors: the amount and quality of protein in the diet; the antecedent nutritional status of the obese subject, particularly with respect to protein and fat stores; the number and source of nonprotein calories (at low levels of energy intake, carbohydrate spares protein better than fat does); the quantity of potassium and other mineral elements taken concurrently; and the amount of time the subject has had to adapt to the new regimen. There is growing evidence that, after an initial phase of nitrogen deficit lasting 1-2 weeks, nitrogen equilibrium can be maintained for some weeks in obese persons who consume a diet restricted to 1-1.5 grams of protein per kilogram of desirable body weight per day, plus supplementary potassium, vitamins, and other minerals. But it is not yet clear whether nitrogen equilibrium can be sustained when such a diet is followed for much longer periods, nor is it known whether body protein will be spared more effectively with some combination of protein and carbohydrate than with protein alone.

While balanced, low-calorie diets providing 800 calories or more per day can generally be used with safety, hypocaloric, low-carbohydrate ketogenic diets have potential side effects, of which both physician and patient should be aware. These include weakness, apathy, fatigue, nausea, vomiting, dehydration, postural hypotension, and occasional exacerbation of preexisting gout. Although they cause discomfort, these symptoms are rarely, if ever, of a serious nature.

Control of Energy Expenditure

Use of Exercise in Treatment

Some studies have shown an inverse correlation between fatness and activity level, demonstrating that decreased physical activity rather than increased consumption of calories seems to be associated with the development and maintenance of obesity. In one study of adults, almost 40 percent of the cases of obesity occurred simultaneously with diminished activity. Obese women have been shown to be less active than nonobese controls. Obese girls and boys consume approximately the same number of calories as nonobese controls while demonstrating decreased levels of activity. The range of energy intake in thin muscular and obese children is similar.

Following appropriate physical conditioning, plasma insulin levels decrease while sensitivity to insulin increases in peripheral tissues such as adipose tissue and muscle. Plasma cortisol and triglycerides decrease and plasma glycerol increases. During exercise, muscle temperature increases and may reach levels as high as 109° F. Muscles exhibit increased oxygen consumption and fibrinolysis is increased. Blood flow through the kidneys and gastrointestinal tract decreases. Prolonged physical training causes stroke volume of the heart and blood volume to increase, decreases the response of heart rate to work load (a difference of some 40 beats in matched control subjects), and increases the capacity of the heart and tissues to extract oxygen from blood. Other beneficial effects of exercise include a decrease in adipose tissue mass, along with a slight decrease in average systolic and diastolic blood pressure. Physically active people tolerate coronary atheromata better.

Lack of physical activity is associated with detrimental effects on body metabolism. Twenty days of bed rest in trained men produced a decrease in red cell mass, plasma volume, and intracellular fluid volume. Loss of body calcium occurred. There was replacement of loose connective tissue with dense tissue, so joint mobility was considerably restricted in less than 1 week. Heart rate increased, and nitrogen balance was generally negative. It took 55 days of intensive training to bring this group of men back to pretest levels.

There is, however, no evidence that physical activity causes changes in glucose tolerance. In most cases, appreciable weight loss does not occur in obese populations subjected to physical training without dietary restrictions. Increased mobilization of cholesterol may take place, but physical training does not lower blood cholesterol concentrations. In human beings, few, if any, changes in coronary collateral circulation occur as a result of training, although peripheral blood flow is improved. Obese women have demonstrated no increase in weight loss with exercise (walking) unless they have spent more than 30 minutes per day in this activity. It may be easier to eat 350 fewer calories per day than to expend an extra 350 calories per day in exercise.

Moreover, increased physical activity has hazards. Sweating produces loss of extracellular fluid. Circulating blood volume decreases. A tendency toward more rapid blood clotting occurs. There is decreased blood flow through the kidneys and gastrointestinal tract. A sudden increase in physical activity can be hazardous to persons with coronary artery disease. Joint and foot problems can result from increased physical activity, and, in hot weather, heat stroke can occur.

Nevertheless, exercise can be used in the treatment of obesity in both children and adults. In the case of children, individual skills should be developed to stimulate a desire to be physically active. A daily program of physical education is needed to develop sports skills and physical fitness in all schoolchildren, not merely in athletically gifted males.

Adults should undertake a type of physical activity they can do well and enjoy. Obese persons are as skillful as nonobese in walking. Exercise need not require a special environment, such as a gymnasium. Activity should be incorporated into daily schedules. Walking may be the best exercise to start with, and more sophisticated types of activity can be employed later, depending on the individual's progress.

Behavioral Therapy

Ten years have elapsed since Stuart published the results of the use of behavior modification techniques in the treatment of obesity (143). During this period there has been a virtual explosion of studies using these techniques.

Although reports of behavioral therapy are promising, Mahoney (107) has recently stated: "The fact that behavioral strategies are more effective than others does not imply that they are therefore very effective. We remain a long distance away from any semblance or justification for complacency in weight regulation. Significant poundage losses are still in the minority and long-term maintenance has been seldom examined."

It appears that many behavioral scientists initially fell into the all-too-common trap of assuming that all obese people behave similarly, and that a simple approach based on cue suppression could quickly produce changes in eating behavior that would result in rapid and permanent changes in body weight. This assumption led to nonindividualized approaches and failure to discriminate between patients on the basis of age of onset, fat distribution, level of obesity, and other individual characteristics. Also, the earlier programs were of short duration, usually 8-12 weeks. We now recognize that it was unrealistic to expect enduring changes to be made in such short periods of time. More recently, programs of longer duration, including a variety of modules directed at attitude and lifestyle change as well as at eating behavior, have been reported. An individualized behavioral approach does offer considerable promise for the effective treatment of obesity.

The behavioral approach has a number of noteworthy characteristics:

- Dropout rates tend to be very low in programs that do not try to create an aversion to food. Behavioral strategems such as fee schedules and contracts probably are responsible for the high rate of adherence, although the humanistic, nonpunitive approach may also be appealing to many patients.
- There tends to be great variability in weight loss between patients suggesting either that there is a category of obese individuals who benefit greatly from changing their eating behavior or that treatment is not sufficiently individualized.
- The aversive programs (those that employ punishment to create an aversion to food) are characterized by high dropout rates.
- Self-control programs tend to be more effective than external control or aversive programs.
- The longer the treatment, the greater the weight loss.
- Finally, in contrast to most other therapies, there are almost no reports of untoward or adverse reactions to weight loss resulting from this form of treatment.

Community-Based Programs

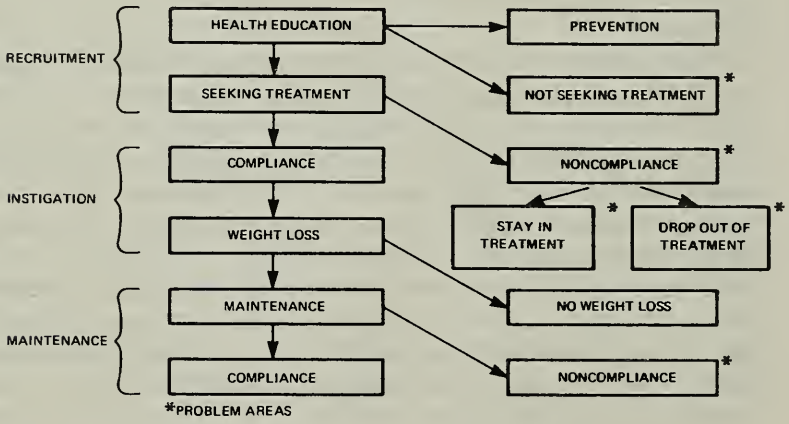
Community-based weight control efforts are justified on the supposition that they offer more opportunities for a wider variety of activities than do programs restricted to traditional medical settings. Opportunities for diffusion of information and for enhanced social support for change are greater if the entire community is involved in the effort. Schools, workplaces, and the home, as well as traditional health care settings, may be proper sites for educational programs. Nonprofit organizations, as well as mass media outlets and educational institutions, may be enlisted in a change effort.

The Stanford Heart Disease Study (43) was based on this kind of broad involvement and achieved considerable reduction in the total number of cardiovascular disease risk factors in the populations over a 2-year period. Obesity control was included as one of the many subgoals in an educational campaign. Dietary changes and reductions in blood pressure, smoking, and plasma cholesterol were achieved in all subgroups within the treatment communities, and these changes were stable over the 2-year period. Weight reduction was achieved only in a subgroup of individuals who received not only generally mediated instruction, but also supplemental face-to-face skills training. In recent concurrent studies, however, it has been found that, for patients with ingrained poor health habits, mediated methods can supplant much of the instruction heretofore delivered more effectively by face-to-face methods.

The Problem of Adherence to Regimes Designed for Weight Reduction

From the Therapist's Standpoint

Regardless of the type of treatment used, a successful outcome requires compliance at numerous stages of the therapeutic program. Some of the critical points are outlined in the following diagram:



Studies of compliance in relation to a variety of public health problems indicate that 40-50 percent of the subjects do not follow advice. These figures apply to obese individuals as well. Possible ways of improving compliance include: 1) improving communication techniques; 2) manipulation of situational variables; 3) conducting higher order treatments, i.e., procedures designed to increase the probability of compliance and not aimed specifically at obesity control per se, e.g., performing behavior modification procedures designed to effect accurate medicine taking, or increasing the palatability of diets, or making access to exercise easier; and 4) capitalizing on individual differences.

Evidence already indicates that significant gains can be achieved by attending to these variables and that variables effective at one stage are not necessarily effective at others. Examples are given in the following brief table:

Effects

Variable	Stage			
	Recruitment	Instigation	Maintenance	Dropout
Sidedness	Yes	No	?	No
Self-Control	?	No	Yes	?
Experience of fear	No	Yes	?	No

From the Patient's Standpoint

The results of a survey of more than 2,000 obese persons who had tried a variety of weight-reduction regimens, often under medical supervision, can be summarized as follows:

- Receipt of a specific diet and/or pills from their doctor was more satisfying than vague instruction to limit food intake. Patients given such specific treatment also were much more likely to be asked to report back to their doctor for followup at regular intervals.

- When asked to rate the various weight-reduction programs they had tried, men rated diet alone as the best method for quick, permanent loss. On the other hand, women rated pills as the best method for quick loss and group treatment as the best method for permanent loss.

- When asked to rate the various methods of dieting they had tried, patients listed calorie counting, carbohydrate counting, and following a diet that listed foods under different categories. The least popular diets were starvation and "set" diets (those that dictated meals to the patient). Women tended to prefer calorie-restricted diets; men tended to prefer carbohydrate-restricted diets.

8

Treatment of Obesity with Drugs and Invasive Procedures

George A. Bray

Since obesity does not have a statistically significant effect on an individual's life expectancy until he or she is more than 30 percent above desirable weight, any medication designed for persons less than 30 percent overweight must be essentially free of risk. The ideal agent for this purpose ought to be free of long- and short-term toxicity, be well tolerated, allow titration of body weight to a desired level, have no deleterious metabolic effects, and be inexpensive. No such agent is currently available. In the following paragraphs, we will examine some of the pharmacologic agents now in use as adjuncts for the treatment of the obese patient. We shall also discuss some of the drugs that have been considered for this purpose but abandoned, and some newer approaches that may be fruitful in the future.

Pharmacologic Approaches To Treating the Obese Patient

Drugs That Act on the Central Nervous System To Suppress Appetite

Amphetamines and Related Agents

In most instances anorexigenic drugs are chemical derivatives of phenethylamine. They possess many of the pharmacologic properties of the naturally occurring adrenergic hormones, epinephrine and norepinephrine. Several chemical modifications have been useful in dissociating the effects of these drugs on the cardiovascular system and on the excitability of the central nervous system from their effects as appetite suppressants.

TABLE 1.--Anorectic agents currently employed for the treatment of obesity in the United States

Generic name	Proprietary name	DEA schedule[a]
d,l-Amphetamine	Benzedrine and others	II
Methamphetamine	Desoxyn and others	II
Phenmetrazine	Preludin	II
Phendimetrazine	Plegine	III
Benzphetamine	Didrex	III
Chlorphentermine	Pre-Sate	III
Clortermine	Voranil	III
Mazindol	Sanorex	III
Fenfluramine	Pondimin	IV
Diethylpropion	Tenuate, tepanil	IV
Phentermine	Fastin, ionamin (resin)	IV

[a] Drug Enforcement Administration: The schedules of the Controlled Substances Act are numbered in order of decreasing potential for abuse; drugs in Schedule II (amphetamine, methamphetamine and phenmetrazine) are the most restricted.

All the drugs listed in table 1 can increase locomotor activity and stimulate the central nervous system, but their relative potency differs greatly. Amphetamine and methamphetamine are the most potent and fenfluramine the least potent. The latter drug is both a stimulant and a depressant. Increases in heart rate and in blood pressure are the most common of the cardiovascular effects frequently observed with these drugs, which also increase body temperature, dilate the pupils, reduce food intake, and reduce the duration of sleep. Tachycardia is minimal with mazindol and fenfluramine. Amphetamine and methamphetamine are nearly identical on all parameters. Phenmetrazine is one-third to one-fourth as potent as the other two amphetamines on most of the cardiovascular and central nervous system responses. Increasing evidence indicates that amphetamine, diethylpropion, phentermine, and mazindol decrease food intake by a different mechanism from that of fenfluramine; the first group of drugs requires an intact catecholaminergic system, while fenfluramine acts on the serotonergic systems.

To evaluate the clinical usefulness of these drugs, two questions need to be answered: 1) Are they effective? and 2) Are they safe?

The Food and Drug Administration (FDA) has evaluated 105 applications submitted for marketing appetite-suppressing drugs. The applications contain 210 double-blind studies and an additional 145 studies that include two active drugs. The applications contain data on nearly 10,000 patients and provide the most extensive body of information yet assembled on the effectiveness of these agents. The drugs included in the FDA study are listed in table 1, with their trade names and usual dosages. The data analyzed by the FDA covered 4,543 patients treated with active drugs and 3,100 patients treated with placebo. The dropout rate, in studies lasting 3, 4, or 6 weeks, was 18.5 percent for patients on placebo and 24 percent for patients on active drugs. At the end of the study period (3, 4, 6, 8, 12, or 20 weeks), equal numbers of patients receiving placebo and active drugs were retained (49 percent placebo and 47.9 percent active drugs). The weight loss averaged 0.56 pound per week more for patients receiving active drugs than for patients receiving placebo. In other words, a weight loss of 1 pound or more per week was almost twice as common in patients receiving active drugs as in those receiving placebo (44 percent for active drug versus 26 percent for placebo). Similarly, a weight loss of 3 pounds per week was almost twice as common among those receiving active drugs as among those receiving placebo (2 percent of those on active drugs lost 3 pounds per week versus 1 percent on placebo).

Analysis of the data from 145 parallel studies revealed no significant differences between any of the drugs in table 1. Thus in clinically effective doses there was little variation between these compounds in terms of effectiveness or the amount of weight lost. That is, in studies lasting up to 20 weeks in which sufficient numbers of patients were retained, those on any of the active drugs lost significantly more weight than those receiving placebo.

However, the long-term effectiveness of these drugs has never been established. The longest trials in which effective numbers of patients were retained lasted between 20 and 24 weeks. Beyond that time, the dropout rate became too high for effective evaluation.

Although the effects of drugs on weight loss statistically were significantly greater than with placebo, the 1972 Final Report to the Director of the Bureau of Drugs, by Dr. T. Prout, chairman of the consultants on anorectic drugs, interpreted this difference as "clinically trivial." In our view, this interpretation has a serious limitation. The weight loss of patients treated with drugs was greater than that of the placebo-treated group. If the drugs produced a "clinically trivial" effect, then the effect of diet and other modalities prescribed for the placebo-treated patients must also be interpreted as "clinically trivial." This is a dilemma which the regulatory agencies may not wish to have. We think it would be appropriate to delete the concept "clinically trivial" from assessments of this type.

Safety of anorectic agents also has been the subject of considerable discussion. The possibility of enhanced mortality in patients receiving diet pills was brought to public attention in reports by Henry (81) and Jelliffe (89) of deaths in patients receiving these drugs (150). These patients were usually treated with amphetamines, thyroid pills, potassium-depleting diuretics, and laxatives. In some of the patients it would appear that potassium deficiency and the ensuing hypokalemia may have been the major factors leading to death. This possibility remains a potentially serious one, although a review of deaths among patients using amphetamines and thyroid pills in "reasonable doses" could find no evidence of increased mortality (7). An equally serious problem is the potential for developing tolerance and the possibility of drug abuse. Indeed, the latter problem of habituation and addiction to certain "diet" drugs has led to the current criticism of their relative value in the treatment of obesity. If these drugs were not subject to widespread abuse by certain groups in our society, there would be far less concern about their use in treating obese patients.

In addition to their potential for abuse, these drugs carry with them a number of possible side effects. The two most common are insomnia and dry mouth. The others--with the exception of depression and diarrhea, which occur mainly with fenfluramine--are seen in small numbers.

Intermittent therapy can be as effective as continuous use of a drug. Such treatments usually involve an uninterrupted therapy lasting 3-6 weeks, followed by a period of discontinuation lasting at least half as long as the original period of treatment. Intermittent therapy with fenfluramine is inadvisable because of the possibility of postdrug depression. Some diet drugs have been used in children with apparent effectiveness. For example, fenfluramine, chlorphentermine, and diethylpropion produced no statistically significant reduction in the linear growth velocity of children treated for 1 year. However, 17 children treated with mazindol for 1 year had a significant reduction in growth rate.

In summary, it is clear that the agents listed in table 1 can be effective as adjuncts in the treatment of obesity, but their usefulness depends on their inclusion in a total treatment program. The drug abuse potential is higher for those compounds classified in FDA's Schedule II; it would appear reasonable, therefore, to select a preparation from Schedule III or IV. Diethylpropion might merit initial consideration, with phentermine, clortermine, chlorphentermine, fenfluramine, and mazindol in second place. Among patients with a history of depression or mental illness, mazindol, clortermine, and diethylpropion would merit first choice, and fenfluramine probably should not be used. However, fenfluramine might be the drug of choice for diabetics. Mazindol or diethylpropion would appear to merit first consideration for hypertensive patients. The value of intermittent or interrupted courses of therapy should be kept in mind. References 36, 65, 133, 148, and 153 present detailed discussions of individual drugs.

L-dopa

This substance is an intermediate in the synthesis of dopamine norepinephrine and epinephrine. Because L-dopa can enter the brain, it has been used to provide a precursor for dopamine in the treatment of Parkinsonism, a neurological disorder. When dose levels get too high, nausea may occur. Researchers explored the possibility that this drug might be used to produce nausea in obese patients and thus treat obesity. However, patients treated this way did not lose a significant amount of weight; in fact, seven obese women who were given the dopaminergic agent bromergocriptine for 3 months did not show any weight loss.

Gastrointestinal Hormones

A third category of compounds that may act to suppress appetite centrally includes the gastrointestinal hormones released when food enters the small intestine. Cholecystokinin and its synthetic terminal decapeptide have been demonstrated to decrease food intake in both rats and monkeys, but studies in humans have shown only a small effect or have been unable to demonstrate any effect at all.

Calorigenic Drugs

Thyroid Hormones

The first use of thyroid hormones to treat obesity is attributed to Baron (125). In the ensuing 80 years, more than 200 publications have described the administration of thyroid hormones to obese patients. The majority of these studies conclude that either thyroxine (T_4) or triiodothyronine (T_3) produces greater weight loss than does a placebo.

This enhanced weight loss during treatment with thyroid hormones results from two effects of the drug: 1) increased oxygen consumption and 2) increased protein catabolism. In one study, doses of triiodothyronine above 100 micrograms per day consistently increased the metabolic rate of hospitalized obese patients (23). In another study, T_3 was administered to hospitalized obese patients and resulted in increased oxygen consumption and an enhanced rate of weight loss, particularly during the early phases of treatment (84).

It is clear that thyroid hormones induce a number of changes in obese patients that tend to enhance weight loss. Although some of these effects are desirable, others are not. The unwanted effects have been used as arguments against the safety of thyroid hormones in the treatment of obesity. One useful effect is the stimulation of oxygen consumption with increased utilization of endogenous fuel; undesirable effects include the acceleration of protein catabolism and increased nitrogen excretion. Although approximately two-thirds of the extra calories expended as a result of T_3 treatment result from the catabolism of fat, the majority of the early weight loss results from catabolism of protein. Studies have suggested that increasing the protein content of the diet can overcome this catabolic effect.

A potentially more dangerous side effect is the action of thyroid hormone to modify the chronotropic and inotropic properties of cardiac muscle. Although the mechanism for these effects is not known, treatment with thyroid hormones has increased the mass of the heart in experimental animals, and such an effect is likely to occur in humans as well. Since obesity itself increases the work of the heart as well as its size, the added cardiac load imposed by treatment with thyroid hormones could be detrimental.

Finally, any beneficial effect of treatment with thyroid hormone must be evaluated in terms of long-term weight loss as compared with other modes of treatment. Two reports have followed patients previously treated with T_3. In both, T_3 was initiated in low doses and increased stepwise. In one study, the patients were started on treatment in the hospital (60). When they were reevaluated later, 12 percent had maintained a weight loss of 20 pounds or more, and 6 percent had maintained a loss of more than 40 pounds; only 1 of 199 patients had approached ideal weight. This outcome is no better than that achieved with diet alone. A similar conclusion was reached in the second study, which followed 55 patients treated in two groups. Four of 28 in one group had maintained their 20-pound weight loss, and 2 had maintained a 40-pound weight loss.

Growth Hormone

This hormone is important during the processes of growth and differentiation. Its calorigenic effects, however, are less well known, although they have been described in careful studies on panhypopituitary subjects. In experimental animals, growth hormone increases metabolic rate after thyroidectomy, indicating that its calorigenic effects are not mediated through the release of thyroid hormone.

Growth hormone given to obese individuals at a dose of 5 milligrams per day produced a significant increase in metabolic rate (15). The rise in metabolic rate took 1-3 days to occur, but thereafter basal metabolism remained elevated throughout the day. Administration of growth hormone to hypopituitary children has been shown to cause a reduction in skinfold thickness. Further studies in humans await an increase in the available supply of human growth hormone; however, its potential is limited by the undesirable side effect of acromegaly. The recent description of somatostatin, a growth-hormone-inhibiting peptide, and the possibility of isolating a growth-hormone-stimulating peptide, may provide a way to manipulate endogenous growth hormone.

Drugs Postulated To Increase Fat Mobilization

Human Chorionic Gonadotropin

A treatment consisting of diet and chorionic gonadotropin injections has been in use for years. The recommended therapy consists of a 500-calorie diet and 20-40 daily injections of 125 international units of human chorionic gonadotropin (HCG). Weight losses of 9-14 kilograms in 40 days have been reported with this method. The biological functions of HCG are similar to those of luteinizing hormone (LH) secreted by the pituitary. Commercial preparations of HCG are impure and contain minute amounts of a number of other substances. Moreover, the drug has not been approved for use in the treatment of obesity, although the safety of HCG at the doses used in such treatment has rarely been questioned. In one study, basal metabolism, protein-bound iodine (PBI), blood sugar, serum cholesterol, and lipids remained unchanged during treatment with HCG. Several recent clinical trials have provided unequivocal evidence that this drug is no more effective than are placebo injections (70, 140).

Indomethacin

Adipose tissue from obese individuals fails to release free fatty acids and glycerol normally in response to isoproterenol in vitro. It has been shown that prostaglandins E1, E2, and F2 are released in vitro from adipose tissue during stimulation with isoproterenol, and that the release of these same prostaglandins may antagonize lipolysis by blocking the hormone-sensitive lipase. Indomethacin decreases prostaglandins and has been shown to reduce the body weight of normal rats and genetically obese "Zucker" rats and their lean littermates. Indomethacin has not been subjected to trial in humans, but even if such trials were conducted and found successful in creating weight loss, the toxicity of the drug would certainly limit its application.

Drugs That Interfere With Intestinal Digestion and Absorption

The success of intestinal bypass operations as treatment for obesity has led to the search for oral agents that produce a medically reversible form of altered intestinal absorption.

Drugs Blocking Glucose Absorption

Glucose receptors that might depress food intake exist in the intestinal mucosa. Thus, there is the possibility of developing a compound that blocks glucose receptors in the intestinal mucosa, resulting in decreased food intake and weight loss. This pharmacologic approach might yield a drug that would remain within the intestinal lumen and have no systemic effects while effectively inducing weight loss.

Neomycin

Another approach to manipulating intestinal absorption has focused on the possibility of producing decreased fat absorption and steatorrhea. Several groups of investigators have demonstrated that neomycin increases the loss of fat in the stools. In doses of 6-12 grams, this drug consistently produces steatorrhea. It has been demonstrated that a dose as low as 3 grams per day impaired fat absorption in 5 of 10 patients. While the impairment of fat absorption may indeed be applicable to the treatment of obesity, this particular drug is limited by the fact that doses of neomycin that are associated with steatorrhea produce morphologic alterations in the intestinal mucosa. Because obesity is a chronic condition, the possibility that irreversible alterations in intestinal absorption might occur limits the use of this and closely related agents.

Cholestyramine

This drug is an ion-exchange resin that elicits steatorrhea by binding bile acids in the intestine and thus increasing fecal fat excretion. In studies to examine the relationship between cholestyramine and fecal fat excretion, two grossly obese patients were maintained on a 1,200-calorie diet in which 80 percent of the calories were provided as fat. Cholestyramine doses of 36 grams per day were administered to each patient for 9 days. There was a significant increase in fat excretion during the period of treatment with cholestyramine, but the loss of fat in the stools was disappointingly low (16). Another study reported that 30 grams of cholestyramine given daily to six obese patients increased the fecal fat excretion threefold (30). However, this fecal calorie loss was not enough to account for the weight loss, which was thought to be due to nausea. Thus, at present, the available agents for decreasing fat absorption and producing malabsorption have not proved effective in dealing with the problem of obesity.

Amylase Inhibitors

Recent studies suggest that the inhibition of carbohydrate digestion in the intestinal tract by inhibitors of pancreatic α-amylase may provide a possible approach to the treatment of obesity and diabetes mellitus. The rationale for this approach is as follows: Amylase plays a key role in carbohydrate digestion by hydrolyzing starch to maltose, which is further degraded to glucose; since neither starch nor maltose can be absorbed by the intestinal mucosa, the inhibition of amylase prevents the metabolic utilization of starch. BAY d 7791, an amylase inhibitor from wheat, consisting of thermostable proteins with a molecular weight of about 16,000, and BAY e 4609, an inhibitor from microorganisms comprising complex oligosaccharides, have been described in several studies. These inhibitors diminished the intestinal digestion of starch and attenuated the hyperglycemic and serum insulin responses to starch ingestion in healthy volunteers and diabetic subjects (94). The reduced bioavailability of carbohydrate was further demonstrated by the depressed conversion of starch into lipids of adipose and aortic tissues in rats receiving BAY e 4609 orally.

Perfluoroctyl Bromide

The nonselective prevention of food absorption from the gastrointestinal tract has been reported recently. Perfluoroctyl bromide (PFB), a chemically and biologically inert, nonabsorbable fluorocarbon of high molecular weight used as a radiopaque contrast medium, was employed to coat the stomach and intestines of rats and thus reduce nutrient absorption. When administered to rats prior to and during a 3-hour meal, PFB prevented weight gain throughout a 13-day study.

Sucrose Polyester

Sucrose polyester (SPE), a preparation of sucrose with six, seven, or eight of its hydroxyl groups esterified with long-chain fatty acids, is a noncaloric, unabsorbable synthetic fat with physical properties similar to those of dietary triglyceride. The negligible metabolism and absorption of SPE has been confirmed in both rats and humans (41). Since SPE is neither digested nor absorbed, there is the continued presence of an oil phase of SPE in the intestinal lumen. Exogenous and endogenous cholesterol will distribute into this oil phase and be egested in the feces. Each replacement of 1 percent dietary triglyceride with SPE resulted in a 1.2 percent decrease in cholesterol absorption. In normal subjects, treatment with SPE (50 grams per day for 10 days) significantly reduced total plasma cholesterol and low-density lipoprotein (LDL) cholesterol; no changes were observed in hypercholesterolemic subjects. The use of SPE as a weight-controlling agent is suggested by the numerous varieties of food in which conventional fats can be replaced by SPE.

Slowing of Gastric Emptying

Trans-epoxyaconitic acid (TEAA) has been shown to reduce significantly food intake, weight gain, and body lipids in rats. Anorexia and inhibition of hepatic lipogenesis in vivo were demonstrated only by oral administration of the compound; intraperitoneal administration produced no effect on either parameter. The anorectic activity of TEAA appeared to be related to a selective reduction in the rate of stomach emptying. The resultant depressed rate of substrate entry into the body was reflected in reduced rates of fatty acid synthesis and total body fat.

Bulk Fillers

Methylcellulose has been used to suppress appetite because it is hydrophilic and swells in the stomach. However, it swells relatively slowly and would be unlikely to diminish the appetite significantly. Thus, this agent is better used as a laxative than as an anorexiant. In one trial, methylcellulose produced relatively little weight loss in refractory obese patients when compared with placebo or phenmetrazine. More recently, fenfluramine, methylcellulose, and placebo were compared in a double-blind crossover fashion in subjects on a 1,000-calorie diet. Although fenfluramine was effective in decreasing appetite and increasing weight loss, methylcellulose had no more effect than did placebo on either appetite or weight loss. Thus, the use of methylcellulose in a weight reduction program seems questionable.

Metabolic Blocking Drugs

Hydroxycitrate

The D(-)-hydroxycitrate, an isomer of hydroxycitrate, is a potent inhibitor of citrate-cleavage enzyme, which catalyzes the conversion of citrate to acetyl-CoA and oxaloacetate.

This enzymatic conversion stands at a crucial position in the synthesis of fatty acids. When this compound was fed to animals for 11-30 days, it caused a significant reduction in body fat; however, food intake and weight gain were not affected (148). This compound has not yet been tried in human beings, but it offers an avenue for future exploration.

Drugs Used To Treat Special Problems Related to Obesity

Progesterone

Progesterone, a steroid produced by all steroid-producing tissues, is the principal hormone secreted by the ovary during the postovulatory phase of the menstrual cycle. This hormone increases the rate of breathing and, by so doing, produces a mild respiratory alkalosis. For this reason, it was tried in obese patients with alveolar hypoventilation (the Pickwickian syndrome). During treatment with this compound, there was a significant increase in ventilatory capacity and a reduction in the respiratory acidosis associated with alveolar hypoventilation in obese patients. A recent report has confirmed the usefulness of the hormone for this purpose.

Dilantin

An uncontrolled study reported dramatic success in the treatment of compulsive disorders with dilantin and described some subtle changes in the electroencephalograms (EEG) of treated patients (69). Another study (71) scrutinized these observations more objectively; 250 patients attending an obesity screening clinic were given a questionnaire designed to select compulsive eaters. Seven women who scored in the top 20 percent were given EEG's and entered into a double-blind crossover trial of diphenylhydantoin and placebo. The EEG's in this group of women were normal, and diphenylhydantoin produced no more weight loss than did the placebo. One reason for the ineffectiveness of diphenylhydantoin in this controlled trial could have been differences in patient selection. However, the controlled trial would suggest that, if diphenylhydantoin is at all effective in the treatment of compulsive eating disorders, it must be so only among a very select group of patients and, therefore, must have limited application in the treatment of obesity.

Summary

From the foregoing discussion it should be obvious that there presently is no entirely acceptable, safe, and effective pharmacologic agent for treating obesity. The inadequacy of present drugs has spawned investigations into diverse pharmacologic approaches for new drugs. It will be fascinating to watch this development in the treatment of obesity over the next 5-10 years.

Nonpharmacologic Approaches To Treating the Obese Patient

Intestinal Bypass in the Treatment of Obesity

Two considerations provide the rationale for jejunoileal bypass surgery as a treatment for obesity. First, the success of most conservative methods for treating obese patients has a low yield; and second, the risks of morbidity and mortality in grossly obese persons are substantial.

Indications for Bypass Surgery

This operation should be reserved for patients who are substantially overweight [i.e., more than 50 kilograms (110 pounds) above desirable weight]. Patients with complications such as diabetes mellitus, hypertension, pulmonary alveolar hypoventilation (the Pickwickian syndrome), and serious orthopedic problems may qualify at a somewhat lower weight limit because these problems are likely to be ameliorated by weight loss. There is a feeling that operations on patients who are more than 50 years of age may be more hazardous because of increased difficulties in adjusting to the consequences of this surgical procedure. Patients should have faithfully tried other means of losing weight and failed on more than one occasion before being accepted for intestinal bypass surgery. Some authors have suggested that a stable adult lifestyle and emotional state are desirable, but this contention is not supported by psychiatrists who have dealt with these patients (42).

Patients must be able to accept the hazards of the procedure and should indicate this by signing an informed consent which describes the potential risks and benefits of the operation. The possibility of revision and the need to avoid pregnancy for 6 to 12 months after surgery should be clearly outlined. Finally, this operation appears to be appropriate only where an experienced team of internists, surgeons, and psychiatrists is available and where there are appropriate laboratory and intensive care facilities. The high mortality among patients who undergo surgery at hospitals performing only a few procedures of this type provides further evidence that the operation should be limited to larger medical centers that have appropriate facilities and personnel. Patients with renal failure, progressive myocardial disease, inflammatory bowel disease, pulmonary embolization, and progressive liver disease are inappropriate candidates.

Two major types of intestinal bypass are in wide use. In one operation, the end of the distal segment of the jejunum is attached to the side of the ileum near the ileocecal valve (end-to-side or Payne operation). The other operation anastomoses the distal end of the jejunum to the end of the ileum and drains the defunctionalized bowel into the colon with an ileocolonic anastomosis (end-to-end or Scott operation).

Mechanisms of Weight Loss

Food intake. Weight loss seems to occur for two reasons: 1) decrease in food intake and 2) malabsorption of ingested calories. The decrease in food intake after this operation has been observed by several groups of investigators (21) and has occurred after both end-to-end and end-to-side anastomoses. These measured reductions in food intake can account for most of the weight loss observed in patients who have had an intestinal bypass.

Malabsorption. Malabsorption also occurs after intestinal bypass surgery. There is a decrease in the intestinal absorption of fat, nitrogen, carbohydrate, vitamins, and minerals. Studies have reported the loss of calories in the stools rising from 131 Cal per day preoperatively to a maximum of 593 Cal per day postoperatively. This increase produces a small rise in the rate of weight loss. (A net deficit of 450 Cal per day in the stool accounts for a weight loss of 58 grams of adipose tissue per day.)

Potential Benefits From Bypass Surgery

The benefits of an intestinal bypass procedure can be summarized under three headings. First, there is weight loss that is usually permanent. The amounts lost have ranged from 14 to more than 100 kilograms, and patients usually reach a stable body weight between 12 and 36 months after surgery. The rate of weight loss is related to length of the anastomosed intestine, the patient's initial body weight, the length of the total intestine at the time of surgery, and the type of operation.

The second benefit of this operative procedure is an improvement in psychosocial function. Major adjustments may be required of the patient during the postoperative period, and these commonly have emotional repercussions. Patients usually show greater self-confidence and self-esteem, and these changes may become a source of friction with their families. For this reason, it is important for family members to participate in the decision to undertake surgery. As patients lose weight, they often achieve a more accurate and realistic view of their body size, suggesting that preoperative distortions in body image may be reversible. This surgery may break the vicious circle of unrelieved ineffectiveness, guilt, and resignation and may facilitate new hopes and constructive adjustments in these patients.

The third benefit of intestinal bypass surgery is improvement in morbid risk factors: decrease in blood pressure, decline in insulin requirements, and decrease in serum cholesterol and triglycerides.

Complications of Intestinal Bypass Surgery

The list of complications following this operation has steadily grown longer. It now includes not only those problems associated with the surgery itself, but also a growing number of medical complications resulting from the altered anatomy produced by this surgery.

Operative complications. The overall mortality following surgery is approximately 3 percent for the series of 2,500 patients in the literature. This figure varies from no deaths in smaller series to over 11 percent in other series. There are several reasons for these differences: the difference in experience of the surgical and medical team managing these patients; the degree of obesity among the patients; and the presence or absence of complicating diseases. It is clear from a review of the hospitals where these operations are done that mortality is considerably higher in those hospitals where the procedure is performed only occasionally; for this reason, it is recommended that intestinal bypass surgery be conducted only in selected centers. In addition to operative mortality, there are many other surgical complications, including pulmonary embolism, serious wound infection, gastrointestinal hemorrhage, renal failure, and pancreatitis.

Diarrhea and malnutrition. All patients who have have had a jejunoileostomy develop diarrhea. In the early postoperative period, liquid stools may range in frequency from 8 to 20 or more per day and may produce rectal irritation and associated hemorrhoidal pain. There is a gradual decline in the frequency and severity of this problem. After 6 weeks, stools usually range between 4 and 15 per day, and by 6 months, this usually has decreased to between 2 and 6 per day. The diarrhea can be controlled by one of several methods: reducing the amount of bulk or fiber in the diet, administering calcium salts (calcium carbonate), laxatives that absorb water, such as psyllium seed extracts, or diphenoxylate (Lomotil). A modification of the end-to-side method has been used to decrease the amount of bile acids coming into the colon postoperatively. With this approach, the proximal end of the blind loop (jejunum) is anastomosed to the gallbladder; thus, the enterohepatic circulation of bile acids is preserved and less diarrhea results.

In all patients, there is malnutrition of varying degrees, due to the malabsorption of many nutrients. Hypoproteinemia may be profound in some patients, and serum albumin declines in all. There is increased fecal excretion of nitrogen and impaired absorption of amino acids from the intestine. The absorption of vitamin B_{12} is uniformly impaired, and plasma concentrations decline. Plasma levels of vitamin A and vitamin E also are reduced, which may result in night blindness.

Another manifestation of malnutrition and malabsorption is the loss of electrolytes in the stools. Potassium depletion is often marked and may be associated with profound hypokalemia and symptoms of weakness. If diarrhea is severe, loss of calcium and, occasionally, magnesium, can be significant, and tetany has been reported in a number of patients. Excretion of fecal fat increases and may account in part for the increased loss of calcium, which is combined with fatty acids in the stools.

Pregnancy during the first year following intestinal bypass surgery is frequently associated with an exacerbation of the problems of malnutrition. The presence of a fetus with its demands on the mother can lead to nutritional deficiencies that otherwise might not have surfaced.

Liver disease. Liver disease is one of the most perplexing postoperative complications. The majority of obese patients have abnormal liver function preoperatively, and most get worse postoperatively.

Only a small number, however, develop cirrhosis and progressive liver failure. Tests of liver function such as the serum transaminase and alkaline phosphatase frequently show increased levels in the early postoperative period and have not proved useful as a guide to the severity of the liver problem. Liver biopsies have shown that between 1 and 6 months after surgery fat is frequently increased and there may be a deterioration in the histologic appearance of the liver. This usually improves with time, but it is uncommon for liver histology to return to normal.

Syndromes of bacterial overgrowth. Two syndromes of bacterial overgrowth have been documented. The first has been called pseudo-obstructive megacolon. It presents clinically with intermittent abdominal swelling and distention, and usually occurs 1 or more years after the bypass. The intestine can distend so much that abdominal girth may increase 3-5 inches in a matter of 1 hour. Air/fluid levels may be detected by X-ray, and obstruction can be relieved through intubation or with the passage of gas and stool rectally. This condition appears to be related to anaerobic organisms in the small intestine and colon, and temporary relief may be produced with antibiotics effective against the organisms. The second syndrome, called "bypass enteropathy," consists of fever, abdominal pain, and bacterial growth in the intestinal segment. This appears to be less common than pseudo-obstruction.

Renal failure and urinary calculi. Urinary calculi have been reported with a frequency varying between 3 and 30 percent. The mechanism for the increased stone formation appears to reside in the increased absorption of oxalates.

Several techniques have been developed to increase oxalate loss in the stool and thus decrease its absorption. Among them are the administration of calcium, the use of a low-fat diet, and the administration of antacids, particularly the aluminum oxide variety. Accompanied by an increased urine volume, any of these techniques can satisfactorily diminish the likelihood of uric acid stones.

Arthritis. Polyarthritis with migratory arthralgia has been described in up to 6 percent of patients with bypass. These symptoms are usually associated with pain but are only rarely accompanied by joint swelling and effusion. Fingers, knees, and ankles may be involved. Rheumatoid factor, antinuclear factor, and LE (lupus erythematosus) cells have not been detected. In one study, however, cryoprotein complexes against E. coli and B. fragilis were found in the circulation of three patients with an intestinal bypass. These antigens may serve as the basis for an inflammatory response in the synovium of the joint.

Other complications. Three other complications are noteworthy. The first is the increased incidence of tuberculosis in patients who have undergone the intestinal bypass for obesity. Of more concern is an ataxia and motor incoordination noted by one group of investigators which does not appear to result from a deficiency of the B vitamins and, in some instances, may not be completely reversed when reanastomosis occurs. Finally, symptomatic hypoglycemia has been noted in one patient who developed cirrhosis after intestinal bypass surgery.

Reanastomosis

Reanastomosis and restoration of intestinal continuity has been performed in less than 10 percent of the patients. Severe liver disease, an inability to live with the intestinal bypass, and an inability to solve the problems of pseudo-obstructive megacolon have been bases for reanastomosis.

Gastric Bypass in the Treatment of Obesity

The gastric bypass operation is an attempt to induce weight loss by limiting food intake while maintaining normal digestive functions and normal absorption. The original procedure was developed by Mason in 1966; since then, he and others have modified it in several ways. At present, the surgery is generally performed by generating a very small proximal stomach pouch which is separated from the major, distal portion of the stomach by a continuous row of staples across the fundus. Proximal and distal stomach segments, however, remain connected. A gastrojejunostomy is formed along the greater curvature of the stomach, and usually a jejunal loop is formed near the ligament of Trietz, although some surgeons prefer to use a Roux-en-Y technique to reduce bile reflux. With stapling devices, the operation can be completed in little more than 1 hour.

It is thought important that the volume of the resultant fundic pouch not exceed about 60-100 milliliters. Although much larger pouches were considered acceptable with earlier techniques, more extensive weight reduction was achieved by making the pouch smaller. The size of the anastomosis also appears to be critical. To prevent the stomach pouch from emptying too rapidly, the stoma should not exceed 12 millimeters in diameter. Some surgeons elect to make it as small as 6 millimeters. A large stoma produces less weight loss and may cause the "dumping syndrome."

Criteria for Operation

Criteria for selection of patients for gastric bypass surgery are similar to those for intestinal bypass surgery. Possible contraindications are the presence of reflux esophagitis, hiatus hernia, acid peptic disease, or achlorhydria.

Results

The gastric bypass has been performed by a sizable number of surgeons (4,109). At least 1,456 cases have been reported; in these cases, weight loss proceeded at a rate of 0.4-0.8 kilogram per week, and at 1 year, reduction averaged 30-35 percent of baseline weight. More than one-third of the patients lost 50 kilograms or more; one-third lost less than 25 kilograms. Heavier, younger, well-motivated, active patients sustained greater weight losses. Children and adolescents showed normal linear growth after the gastric bypass. The small stomach and the delay in emptying produced in the patients a sensation of satiety after smaller meals, and normal hunger/satiety patterns returned gradually. Benefits resulting from relief of morbid obesity by conventional methods also were observed after the surgery.

Therapeutic Failures

Inadequate weight loss after gastric bypass surgery is thought to be due to an excessively large stoma and to excessively large gastric pouches, which may subsequently dilate further. Revisions have been performed to make pouches and stoma smaller, but further weight losses were often minor and, in a good many cases, nonexistent. Poorly motivated patients intent on "outeating" the gastric bypass can do so if they consume high calorie fluids in excessive quantities.

Mortality and Complications

The overall mortality in earlier reports was 3 percent, but improved techniques have reduced that figure to 1 percent or less. One series of 300 cases showed no deaths (4); one death was reported in a series of 173 patients; and a third series showed an operative mortality rate of 1.5 percent. Although only 9 percent of bypass patients in the latter series were above 50 years of age, 27 percent of the deaths occurred in this group.

Complications peculiar to the procedure itself and to the consequences of altered anatomy and physiology may occur. Anastomotic leaks with peritonitis can develop, with infecting organisms corresponding to the oropharyngeal flora. The stoma may become obstructed, and bezoar formation has been described. Dumping syndrome, diarrhea and constipation, vomiting, reflux esophagitis, stomal ulcer (1 percent), gastritis due to alkali or bile reflux, afferent loop syndrome, and weight loss neuropathy have all been reported. Excessive weight loss has not been a problem.

Possible late difficulties may arise from the fact that the bypassed stomach segment is exposed to bile reflux, which is potentially carcinogenic. In patients with achlorhydria, the potential for bacterial overgrowth exists. Since carbohydrate absorption remains intact, gastric bypass does little to relieve diabetes, and since bile acids are normally reabsorbed, cholesterol levels remain unchanged. The number of patients who regain weight appears to be small.

All in all, if surgical treatment for obesity is elected, the gastric bypass seems preferable because it avoids the complications peculiar to the jejunoileal bypass.

Minor Surgical Procedures in the Treatment of Obesity

Both jaw wiring and acupuncture have been tried in the search for weight loss methods without the side effects of medication or the complications of intestinal surgery.

Acupuncture

With the current interest in acupuncture anesthesia, the use of this procedure to induce weight loss has become popular. Since the classic Chinese acupuncture locations for hunger and the viscera are on the earlobe, patients have been treated with auricular retention needles. They are told to press on the implanted needles a half hour before meals or whenever they feel hungry.

Few studies of the effectiveness of this technique have been published. Three reports have presented data showing weight loss and decreased hunger after auricular acupuncture, but none of them included an adequate control group using "inactive" acupuncture points. One single-blind crossover study of 24 subjects used both "active" and "inactive" acupuncture points; no significant weight loss was found for any of the acupuncture sites used (111). Therefore, more carefully controlled studies are needed to document the effectiveness of acupuncture before it can be recommended as a treatment for obesity.

Jaw Wiring

It has been shown that obese patients substantially decrease their food intake when limited to a liquid formula. Based on this finding, wiring the jaws close together to allow only liquids to pass has been used as a treatment for obesity. Eight out of 19 patients completed a 6-month study and showed an average weight loss of 24 kilograms. In a second study of 17 patients, 11 tolerated the jaw wiring for 6 months and showed an average weight loss of 25 kilograms (129). Followup after the wires were removed suggested that the weight was being regained. Both of these studies reported no serious side effects. Therefore, jaw wiring may be appropriate for inducing acute weight loss in selected patients.

What Should We Demand of a Therapeutic Obesity Study?

We may state confidently that the more difficult it is to treat a disease, the more cures will be advocated. Human obesity is an example. We are seeing an overwhelming mass of reports dealing with a great variety of therapeutic measures. Some are intended to make us optimistic, but most leave us with the general--and no doubt realistic--impression that immediate results are moderate and that long-term success is rare.

The main reason for this depressing state of affairs is, of course, the resistance of obesity to current therapy. Thus, although most therapeutic obesity studies leave much to be desired in scope and design, they are fairly reliable insofar as they point to a poor prognosis for the disease.

However, so much time, effort, and money have been expended in the past, and so much more is likely to be sacrificed in the years to come, that it seems worthwhile to draft recommendations for testing the efficacy of a treatment for obesity, whether it consists of diet, medication, exercise, surgery, or any other approach the future may bring.

In the absence of therapy so convincingly effective and harmless that it would persuade everybody, even in an uncontrolled open trial, there is only one principle to follow: that of the controlled clinical trial. Below are listed some general requirements for such a study, several of which are merely statements of the obvious, while some are especially pertinent to treating obesity:

- An adequate definition of degree of obesity must be included, with stratification with regard to various types of obesity or patient if possible: childhood-onset/ maturity-onset, hypertrophic/hyperplastic, hyperphagic/nonhyperphagic, men/women, moderate/ severe, alcoholics/nonalcoholics, etc.
- The target population should be adequately defined from description of patient sample entering trial. The reasons for patients being included in or excluded from the sample must be stated, and so must the reasons some patients drop out. Otherwise, it is impossible to draw valid conclusions about the target population, much less about obese patients in general.
- A prospective design should be drafted.
- Informed consent is necessary.
- An adequate definition of the proposed treatment(s) must be provided.
- Proper criteria for therapeutic efficacy should be defined. For the purpose of obesity studies, these should comprise not only a substantial weight loss (20 pounds or more) but also the durability of the results as shown through followup after at least 2 years, preferably much longer.
- Study populations should be of sufficient size, possibly stratified for obesity type to minimize individual variations.
- Treatment should be allocated randomly, and control groups should be used. Control groups receive either no treatment or some type of current therapy. Treatment must not be allocated until after irrevocable admission to trial.
- Whenever possible, a double-blind protocol should be used.

- Therapeutic efficacy must be weighed against any possible risks, including minor side effects as well as major complications.

Finally, we all must ask ourselves how bad the quality of life--including all the problems of morbidity and psychosocial maladjustment--actually is that accompanies the conservatively treated, and therefore often unalleviated, condition of obesity.

9

Obesity and the Social Environment: Current Status, Future Prospects

Albert J. Stunkard

This report describes the impact of the social environment on the prevalence of obesity. Its four sections discuss 1) the influence of unplanned and uncontrolled factors such as social class; 2) the planned and controlled influence of behavioral therapies upon individuals; 3) the first applications of these therapies to very large groups of persons; and 4) the future, including some social forces that possibly can be directed toward better control of obesity and of other health problems associated with lifestyle.

The Influence of Social Factors on Obesity

The first evidence of how the large-scale social environment influences obesity was obtained by the "Midtown Manhattan Study," a comprehensive survey of the epidemiology of mental illness (139). The population under study consisted of 110,000 adults ages 20-59 in an area of Manhattan selected because it housed persons of both extremes in socioeconomic status. A cross section of 1,660 persons was selected as representative of the 110,000 by systematic probability sampling. Two-hour interviews were conducted with these subjects in their homes by

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Presented at the Bicentennial Conference on Food and Nutrition in Health and Disease, Philadelphia, Pennsylvania, December 3, 1976. [Ann. N.Y. Acad. Sci. 300:298-320. ©1977, New York Academy of Sciences. Further reproduction prohibited without permission of copyright holder.]

trained observers, who obtained information about the individuals' social and ethnic background and a number of items designed to assess psychological and interpersonal functions, as well as height and weight.

This study showed a striking association between socioeconomic status and the prevalence of obesity, particularly among women (62). Socioeconomic status was rated by a simple score based on occupation, education, weekly income, and monthly rent. Figure 1 shows the strong inverse relationship between socioeconomic status and the prevalence of obesity. Fully 30 percent of women of lower socioeconomic status were obese, compared with 16 percent of those of middle status and no more than 5 percent of the upper status group.

Among men the differences between social classes were similar, but of a lesser degree. Men of lower socioeconomic status, for example, showed a prevalence of obesity of 32 percent, compared with 16 percent among upper-class men.

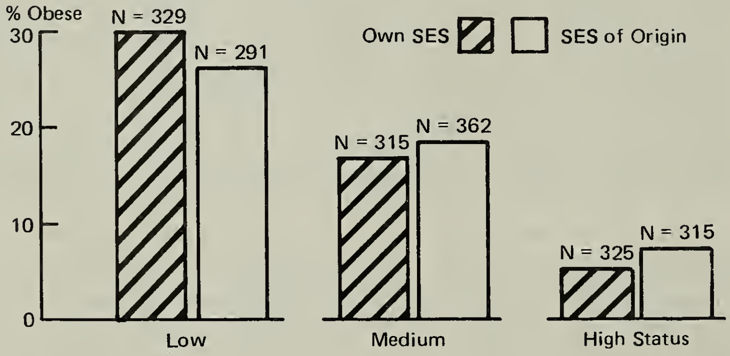
One notable feature of this study was that it was designed to permit causal inferences about the influence of socioeconomic status. This was achieved by ascertaining not only the socioeconomic status of the respondents at the time of the study, but also that of their parents when the respondents were 8 years old. Although a subject's obesity might influence his or her social class, it is unlikely that this could have influenced his or her parents' social class. Therefore, associations between the social class of the respondent's parents and the respondent's disability can be reviewed as causal. Figure 1 shows that such associations were almost as powerful as those between the social class of the respondents and their obesity.

It is remarkable that, in the Midtown Study at least, every social variable investigated was related to the prevalence of obesity, with the relationship usually stronger for women than for men. In addition to socioeconomic status and socioeconomic status of origin, these variables included social mobility, the number of generations of family members born in the United States, and ethnic and religious affiliations.

Obesity was more prevalent among subjects moving downward in social status (22 percent) than it was among those who remained in the social class of their parents (18 percent) and far more prevalent than among those who were moving upward socially (12 percent) (62). Generation in the United States was also strongly linked to obesity. Respondents were divided into one of four groups on the basis of the number of generations that their families had been in the country. Of first-generation respondents, 24 percent were overweight, with the prevalence falling to 22 percent, 6 percent, and 4 percent for succeeding generations.

The presence of nine different ethnic groups in the Midtown Study permitted assessment of the influence of ethnicity on obesity (144). The strongest evidence of this influence was found among persons of lower socioeconomic status, with wide variability about a mean of 30 percent. Ethnicity was not quite as strong a predictor of obesity as socioeconomic status with its 6:1 differential between lower and upper classes; nevertheless, when only lower class

FIGURE 1.--Decreasing prevalence of obesity with increase in socioeconomic status (SES).



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respondents were considered, there was a 3:1 differential between Hungarians and Czechs, who showed a prevalence of 40 percent, and fourth-generation Americans, the least obese group, who showed a prevalence of only 13 percent.

Religious affiliation is yet another social factor linked to obesity (145). Although the sample size precluded adequate control of all relevant variables, the findings nevertheless closely fitted the expected pattern. The greatest prevalence of obesity was found among Jews, followed by Roman Catholics and Protestants. Among Protestants, the pattern was further defined: the largest amount of obesity was found among Baptists, with decreasing prevalence among Methodists, Lutherans, and Episcopalians.

Is this relationship between social factors and obesity an exclusively American phenomenon, or is it more broadly applicable? Two studies have assessed the relationship between socioeconomic status and obesity in London. It should be noted that these studies were based on correlation only--no study since Midtown has gone to such immense pains to determine the social class of the respondents' parents. The close correspondence between the socioeconomic status of respondents and that of their parents in Midtown, however, makes it likely that causation underlies at least part of the correlations found by the London-based studies.

Women of lower socioeconomic status showed a twofold greater prevalence of obesity than did women of upper socioeconomic status (135). Among men the lowest prevalence of obesity was found in the upper class, but there were slightly more obese men in the middle class than in the lower class.

A survey of 1,334 Londoners gave results quite similar to those of the Midtown Manhattan Study (10). Table 1 shows figures for obesity among lower- and middle-class women that are remarkably similar to those of Midtown, with upper-class women showing lower rates, although not quite as low as those in Midtown. It appears that in a Western urban setting, social factors have more influence on women than on men. This inference is supported by the finding that women in the United States have become somewhat thinner during the past 20 years, when concern over women's weight was increasing, while men, subjected to far less pressure, have continued to become fatter.

TABLE 1.--Prevalence of obesity (percent) in London Survey

	A & B	C	
Women	16	18	36
Men	12	16	18

Figures are the percentage of obese persons in each social class. A & B = upper, C = middle, D & E = lower social classes.

[Source: I. M. Baird et al. Practitioner 212:706-714, 1974.]

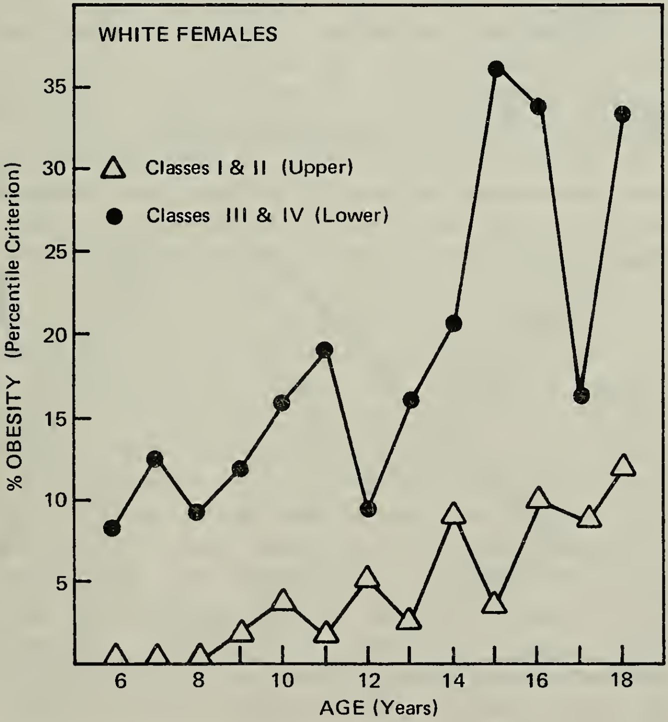
Onset of Social Influences

The consistent and striking relationship between social factors and obesity has led three groups of researchers to investigate the vital question of the age at which this influence makes itself felt. The first of these studies found the same inverse relationship between socioeconomic status and obesity well established by adolescence (86). Among girls, 11.6 percent in the lower class were obese, compared to 5.4 percent in the upper class. Comparable figures for boys were 6.2 percent and 2.3 percent.

The second study also found a decrease in obesity with increasing social status in London schoolboys ages 7-15 (154). Skinfold thickness measures revealed that 8.5 percent of the lower-class boys were obese, compared with 5.1 percent prevalence of obesity among middle-class boys and 4.9 percent among those in the upper class. Interestingly, the study showed no relationship between social class and mean skinfold thickness, suggesting that there is no general increase in fatness among lower-class boys, but rather an increased proportion of definitely obese individuals.

The third study, which reported on 3,344 white schoolchildren in three Eastern cities in the United States, provides conclusive evidence on the influence of social class on obesity in children and gives further disturbing indications of just how early this influence is exerted (146). Figure 2 shows that at age 6 the lower socioeconomic group contained 8 percent obese girls, while the upper-class group had no obese girls at either age 6 or 7. This difference was maintained until age 18, with a rise in the prevalence of obesity with increasing age in both groups. The slopes for the upper

FIGURE 2.--Greatly increased prevalence of obesity among lower-class white girls compared with upper-class white girls.



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and lower classes differed, with the greater yearly increment in the percentage of obese girls occurring in the lower class. Obesity is thus not only more prevalent among lower-class girls, but its greater prevalence is established earlier and increases more rapidly than it does among upper-class girls. Lower-class boys showed greater prevalence of obesity than did those of the upper class, but the differences were neither as large nor as consistent as those among girls.

Influence of Social Factors in Less Affluent Societies

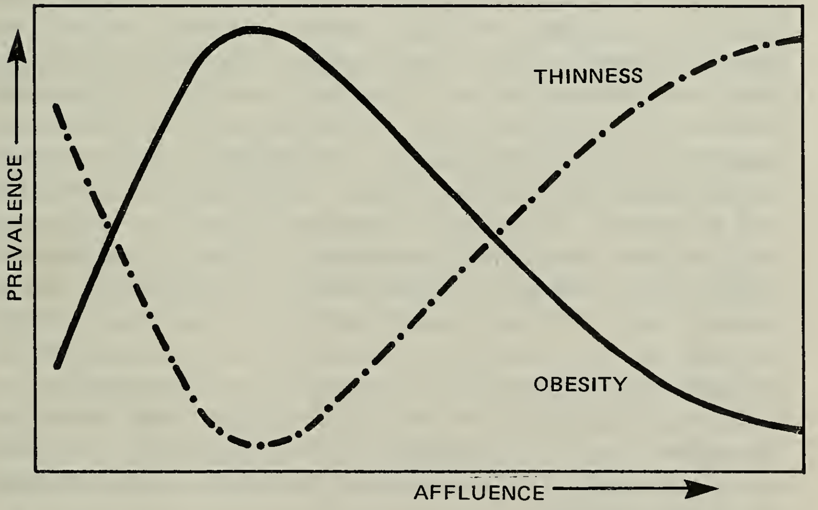
Until recently, we have had no information on the relationship between social factors and obesity in a nonaffluent developed society. This lack is unfortunate, for such information is essential to an understanding of this most potent force. Are the obesity-controlling effects of increasing socioeconomic status in New York a general phenomenon or only a special case in an affluent society?

There is highly suggestive evidence that New York is indeed a special case. Scattered information on the relationship of social factors and mean body weight or mean skinfold thickness (not obesity) in developing countries reveals a relationship precisely opposite to that in Western urban society. Among adults in India, Latin America, and Puerto Rico, and among children in South China and the Philippines, an increasing standard of living is associated with increasing mean body weight or skinfold thickness. The first data on the relationship of social factors to obesity (as opposed to mean body weight) in a less affluent society have been obtained recently in a study of Navaho children. They show that in this setting affluence is directly related to the prevalence of obesity, in sharp contrast to the relationship found in Western urban societies (55). This influence is stronger among boys than among girls, as is an equally strong inverse relationship between affluence and the prevalence of thinness.

Comparison of the standard of living among Navaho children and among children in the Western-city study reveals that the least affluent city children enjoyed a considerably higher standard of living than did the most affluent Navaho children. These findings permit us to construct a general proposition concerning the relationship of affluence and its associated social factors with the prevalence of obesity. Figure 3 shows a maximum prevalence of obesity occurring among the poor members of Western urban society. This prevalence decreases with both decreasing and increasing affluence, but the reasons for the two decreases differ dramatically. With decreasing affluence, the constraint upon the development of obesity is a lack of food. With increasing affluence, fads and fashions exert the control. Information on the relationship of affluence to thinness, although less detailed, shows a pattern that is the mirror image of that for obesity.

The full implications of these findings on our understanding of obesity and on its control have yet to

FIGURE 3.--Schematic of the relationship between affluence and prevalence of obesity and thinness.



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be realized, for they mean that whatever its genetic determinants and biochemical pathways, obesity is to an unusual degree under societal control. They also suggest that a broad-scale assault on obesity need not await further knowledge of its biochemical determinants. Understanding of its social determinants may be sufficient. Such understanding has been greatly advanced by recent studies of the influence of behavioral therapies.

The Influence of the Behavioral Therapies on Individuals and Small Groups

It is unconventional to look at therapy as a form of the social environment, but the introduction of behavior modification for the control of obesity in 1967 has made such a view entirely appropriate. For behavior modification is an attempt to construct a special kind of environment--social and material--to help obese persons gain control over their eating.

The distinguishing characteristic of the various methods called behavior modification is the belief that behavior disorders of the most divergent types are learned responses and that modern theories of learning have much to teach us regarding both the acquisition and the extinction of these responses. Furthermore, proponents of behavior modification have been distinguished by their explicit statements of methods and goals and by their willingness to put their results on the line for comparison with different methods of treatment. Behavior therapists, for example, were among the first to recognize the power of weight change as a dependent variable in psychotherapy research, and they have turned to the treatment of obesity in increasing numbers to utilize this measure. No other dependent variable in psychotherapy research comes close to the sensitivity, reliability, and validity of weight change.

In the past it was fairly easy to assess the effectiveness of any outpatient treatment for obesity, because the traditional results have been so uniformly poor and the treatments so obviously inadequate.

(Inpatient treatment, with its potential for greater control over the patient, has of course been more successful in weight reduction. Its usefulness has been limited, however, by the almost invariable regaining of weight after discharge. Intestinal bypass surgery shows great promise for treatment of severely obese persons, but the number and severity of side reactions limits its applicability.) Only 25 percent of persons entering conventional outpatient treatment for obesity lose as much as 20 pounds and 5 percent as much as 40 pounds.

Against this background, Stuart's report on "Behavioral Control of Overeating" (142) stands out. It describes the best results yet obtained in the outpatient treatment of obesity and constitutes a landmark in our understanding of this disorder. Even the absence of a control group does not vitiate the significance of its findings. The 8 patients who remained in treatment out of an original 10 lost large amounts of weight: 3 lost more than 40 pounds and 6 more than 30 pounds.

Certain features of this report highlight its significance. First, the expenditure of time was not exorbitant. In fact, time spent in treatment was no greater than that in a number of other studies which achieved far poorer results. At the beginning of the treatment period, patients were seen in 30-minute sessions held three times a week for a total of 12 to 15 sessions. Thereafter, treatment sessions were scheduled as needed, usually at 2-week intervals for the next 3 months. Subsequently, there were weekly sessions and finally "maintenance" sessions as needed. The total number of visits during the year varied from 16 to 41.

There was no evidence of untoward responses to the program or of "symptom substitution" (wherein the patient develops new psychosomatic symptoms, apparently in response to the weight loss). Seven of the eight patients reported that they had developed an increased range of social activities, and three out of the six married patients reported more satisfying relationships with their husbands. Furthermore, three of the eight who were also smokers applied the same general program to smoking and either substantially reduced or eliminated it.

A description of the essential elements of behavioral treatments for obesity is beyond the scope of this report, and the interested reader is referred to the extended descriptions by Ferguson, Mahoney and Mahoney, and Stunkard and Mahoney (45, 107, 147).

The behavioral approach, which made it possible to specify treatment conditions rigidly, and the dependent variable of weight change, which made possible fine dissection of the results, have resulted in an explosion of research on behavioral control of obesity. Soon after Stuart's program, a controlled-outcome study based upon that landmark investigation reported an average weight loss of 10.5 pounds among moderately overweight women college students (76). Subjects in a no-treatment control group gained 3.6 pounds, a difference significant at the 1-percent level.

A no-treatment control group was quite acceptable in psychotherapy research in 1969, but it has serious disadvantages. Refusing treatment to someone who has sought it is far from a neutral action. Moreover, disappointment in their expectations for treatment may lead to further deterioration in the condition of members of a control group, which in turn may give the false impression that the therapy used for the treatment group was effective. The problem calls for the use of a placebo control group that receives the same kind of attention and interest given to patients in the active treatment program.

An elaborate study by Wollersheim provided precisely such controls and opened new vistas of psychotherapy research (158). The study's elegant factorial design contained four experimental conditions:

1. "Focal" (behavioral) treatment.
2. "Nonspecific therapy" to control for factors such as increased attention to the patient, "faith" in the treatment, expectation of relief, and the patient's understanding of the treatment rationale. This therapy was carried out in groups that explored

psychological issues related to the patient's obesity but avoided specific behavioral considerations.

3. "Social pressure" was patterned after that of the self-help group TOPS (Take Off Pounds Sensibly) and included such TOPS procedures as a weigh-in, followed by praise for weight loss and encouragement for failure to lose weight.

4. A "no-treatment weight control" group of persons who were promised treatment but received it later.

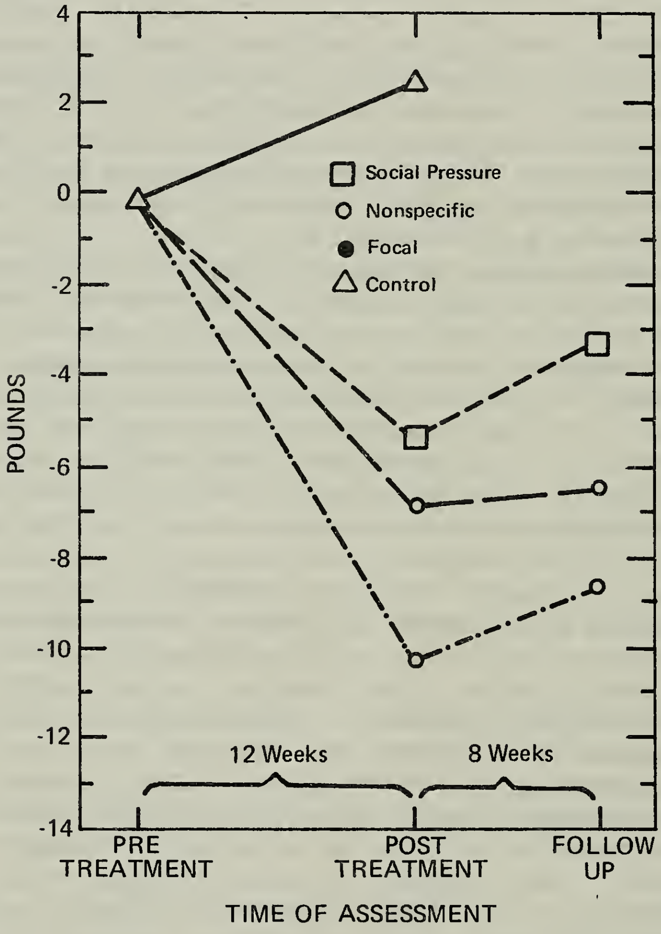
The study thus contained three treatment conditions (1, 2, and 3) and three control conditions (2, 3, and 4) for behavior modification. The 80 subjects were mildly (29 percent) overweight female college students. Four therapists each treated one group of 5 subjects in each of the 3 treatment conditions for 10 sessions over a 3-month period.

Wollersheim's findings are illustrated in figure 4. At the end of treatment and at a followup at 8 weeks, subjects in the behavioral treatment group had lost more weight than those in the no-treatment group. In addition, they had lost significantly more weight than those in the two placebo control groups, which had themselves both achieved respectable weight losses.

Clearly, the behavioral treatment contributed something to the outcome over and above the usual effects of psychological treatment. This contribution seems to have resulted specifically from the behavioral intervention, as evidenced by the fact that, in a detailed eating-pattern questionnaire, subjects in the focal therapy group reported major changes in their eating behavior. Statistically significant differences between the focal therapy group and the other three groups were found in four of the six factors assessed by the questionnaire: "emotional and uncontrolled eating," "eating in isolation," "eating as a reward," and "eating between meals." Whatever caused the weight loss in the two placebo control groups apparently did so without affecting these behaviors. Behavioral therapy apparently produced weight loss by means of its ostensible rationale.

This precedent-breaking study brought psychotherapy research face to face with a problem resulting from the increased maturity of the field: experimenter bias. Although the placebo therapy controlled for the patient's expectations of treatment,

FIGURE 4.--Mean weight loss of the food (behavioral) treatment group, the two alternative treatment control groups, and the no-treatment control group.



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it did not control for the therapist's. This is not a trivial matter. The double-blind experiment in psychopharmacology has shown how powerful this influence can be in dealing with drugs, and it is surely more powerful in the more emotional case of the psychotherapies.

The problem of experimenter bias was approached in an ingenious manner in the study by Penick et al., which was also one of the few to deal with severely (78 percent) overweight persons (122). Therapists for the control group were selected on the basis of their skill in treating obesity and their use of the entire conventional therapeutic armamentarium, including medication. Behavior modification, on the other hand, was carried out by persons with no previous experience in treatment. Fifteen patients were treated with behavior modification and 17 by conventional therapy, both on a once-a-week basis for 2 hours over a period of 3 months. The results favored the behavioral approach. Weight losses among members of the control group were comparable with those in the medical literature: none lost 40 pounds, and only 24 percent lost more than 20 pounds. By contrast, 13 percent of the behavior modification group lost more than 40 pounds and 53 percent lost more than 20 pounds.

Variability in the weight losses of the behavior modification subjects was considerably greater than that of the patients treated by traditional methods. The five most successful patients were in the behavior modification group, as was the single least successful patient. Such greater variability has in other circumstances been associated with greater specificity of treatment, and this explanation of the findings seems reasonable. It appears that for half of the patients, behavior modification offered something specific that resulted in greater than usual weight loss. For the other half, it seemed of considerably less value.

The most important implication of the Penick study lies in its promise of greater applicability of the behavioral therapies. It showed that behavior modification, devised by a team with little experience in the modality, was more effective in the treatment of obesity than was the best alternative program that could be devised by a research team with extensive experience in treatment of this disorder. In fact, the inexperienced therapists achieved about a twofold increase in the effectiveness of their treatment over conventional therapies. Lesser increases in effectiveness have brought about major changes in the management of other disorders. This conclusion naturally leads to the question: How can the advantages of behavior modification be exploited most effectively?

Influence of Behavioral Therapies and Other Measures on Large Groups

Self-Help Groups

A century and a half ago, deTocqueville described the proclivity of Americans to organize informal groups to achieve ends that are the responsibility of government in other societies. Nowhere is this proclivity more impressively expressed than in the organization of patients to cope with common illnesses. Patient self-help groups, pioneered by Alcoholics Anonymous, are attracting increasing numbers of persons suffering from an increasing variety of conditions. One of the largest and most effective of these groups is TOPS, a 25-year-old organization that enrolls more than 300,000 members in 12,000 chapters in all parts of the country. TOPS appears to offer a promising vehicle for the introduction of behavioral techniques, and a recent feasibility study confirmed this promise (103). The study involved all 298 female members of 16 TOPS chapters situated in West Philadelphia and its adjacent suburbs.

The average subject was a 45-year-old woman who had been a member of TOPS for 3 years and who had lost 11 pounds during her membership. She currently weighed 180 pounds, 42 percent above her ideal weight. The homogeneity of TOPS membership permitted remarkably close matching of subjects in the different treatment conditions.

Four treatment conditions, each containing four TOPS chapters, were employed for a total of 12 weeks:

- Behavior modification carried out by professional therapists.
- Behavior modification carried out by the TOPS chapter leader and coleader, who had each received brief training in the procedures and who used the same manual as that used by the professional therapists.
- Nutrition education provided by chapter leaders who had received an amount of training in this area comparable with that provided the chapter leaders in behavior modification.
- Continuation of the standard TOPS self-help techniques.

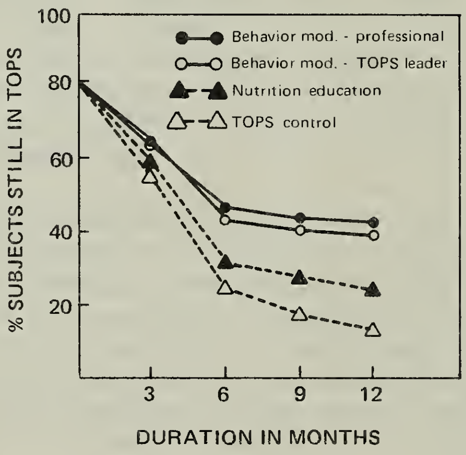
TOPS shares with the medical treatment of obesity the problem of very high dropout rates. The first major finding of this study was that far fewer subjects dropped out of the behavior modification programs compared with subjects in the nutrition education and control groups. Figure 5 shows that the attrition rate in the two behavior modification conditions was lower during treatment and significantly lower at a followup 1 year later. At followup, 38 percent of one group and 41 percent of the other had dropped out of the behavior modification programs, compared with 55 percent for the nutrition education and 67 percent for the standard TOPS program.

Despite the bias against behavior modification resulting from the differential attrition rates, behavior modification produced significantly greater weight loss than did the control conditions. Members in professionally led chapters lost an average of 4.2 pounds, compared with an average loss of 1.9 pounds among members of the TOPS leader-led chapters. The nutrition education chapters showed no change in weight, while chapters receiving the standard TOPS program actually gained 0.7 pound. The relative superiority of the behavioral treatments increased at a followup at 1 year. Chapters with professional leadership continued to show lower attrition rates and weight loss, to a total of 5.8 pounds. The initial weight loss of the subjects in the behavior modification programs conducted by TOPS leaders was not maintained during followup, but these subjects did better than those in the nutrition education and control groups, who gained significant amounts of weight.

This has been an important feasibility study. We now know that behavior modification can be introduced into large population groups through appropriate institutional auspices. The next step is to improve the performance under these conditions and to find institutions willing to introduce the techniques.

TOPS, it appears, will not be such an institution. It has made no effort to capitalize upon the program to which it made such a significant contribution. Ironically, the chief beneficiaries may well be TOPS' arch rivals, the commercial organizations such as Weight Watchers.

FIGURE 5.--Attrition rate of TOPS subjects over a 1-year period under four experimental conditions.



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Commercial Enterprises

There has been little scientific investigation of commercial weight reduction enterprises; what we know about them is largely anecdotal and impressionistic. This situation is now changing, however, and the next few years will doubtless bring an objective appraisal of this rapidly developing area.

By far, the largest and most successful of the commercial enterprises is Weight Watchers International, which since its establishment in 1963 has grown to serve more than 400,000 people each week in the United States and in 25 foreign countries.

The vast Weight Watchers organization is operated on a decentralized basis through a number of semiautonomous franchises. It retains much of its operating format as developed by its founder, Mrs. Jean Nidetch. Its program content has been strengthened over the years with the additions of a medical director, professional nutritionists, and a psychological director. Its members meet weekly for about 1 hour in groups of varying size. They are weighed privately and then participate in a class led by a Weight Watchers employee who has already achieved weight loss.

The food plan used by Weight Watchers originally followed very closely the diet developed by Dr. Norman Jolliffe, of the New York Department of Health (91). In the late 1960's, this diet was substantially modified to increase the volume and number of foods permitted. It has recently been further modified to provide a greater variety of foods in a nutritionally balanced diet, with specialized food plans offered to those who reach plateaus in weight loss and to those who have achieved their weight loss goals.

In 1974, after a period of careful planning, a program of behavior modification was introduced into Weight Watchers on a broad scale by Dr. Richard Stuart, who had initiated the explosion of research in this area 9 years earlier (143). The program is presented in 18 general-purpose and 5 special-purpose "modules." Each module contains a rationale, several specific recommendations for changes in behavior, and a means of charting progress in those changes. Modules are presented in class, and members' progress in the recommended steps is discussed a week later. Introduction of these modules is reported to have increased the average weekly weight loss in groups selected for special study.

The application of the behavioral weight management program on such a large scale stands as one of the major social experiments of our time, and is the first approach to the control of obesity that is broad enough to warrant description as a public health measure.

Medical Auspices

Until quite recently, traditional public health efforts in the field of weight control have been conspicuous by their absence. However, a pilot study of a highly integrated health change program which included weight control has been reported by the Stanford Heart Disease Prevention Program (Three Community Study). That program was carried out in three California towns of 14,000 persons each, remarkably well matched in a variety of demographic variables (43). One town served as a control; the other two were subjected for 2 years to a highly sophisticated media campaign that included about 50 television and 100 radio spots; 3 hours of television and several hours of radio programing; columns, stories, and advertisements in the weekly newspapers; posters and billboards; printed material sent via direct mail to participants; and other assorted materials. The dominant characteristic of the media campaign was its organization as a total integrated information system based at first on data gathered from preliminary surveys and later on information gathered during the course of the programs. In one of these towns the media campaign was supplemented by a face-to-face instruction program directed at two-thirds of the participants in the top quarter of the population at risk for coronary heart disease. These 107 men underwent a behavior modification program once weekly for a

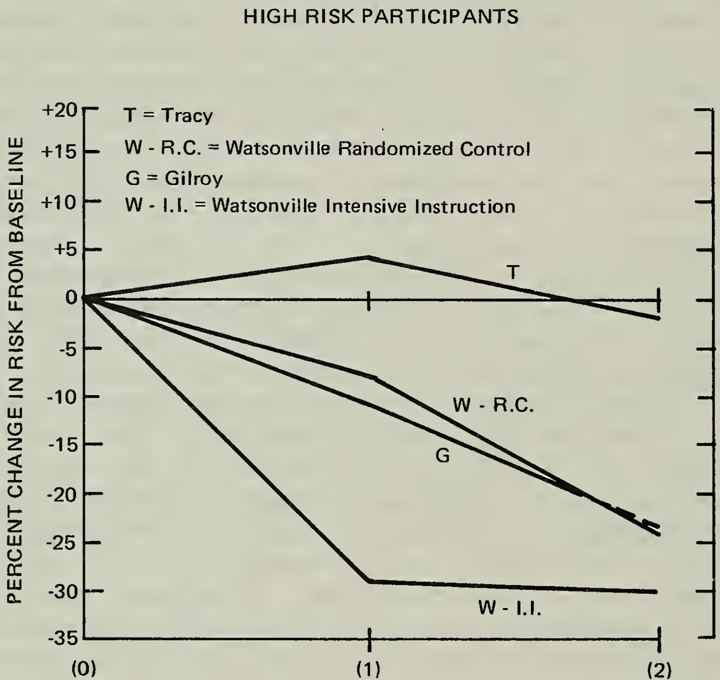
10-week period during the 1st year and a less intensive program during the 2d year.

The goal of the program was to reduce the risk of cardiovascular disease by changing the information available, as well as individuals' attitudes and behavior--changes that would lead not only to weight reduction but also to reduction in intake of saturated fats, cholesterol, and salt; cessation of smoking; and increase in physical activity. Both alone and combined with face-to-face instruction, the media campaign produced highly significant changes in all three areas: knowledge, attitudes, and behavior. By the end of the 2d year, risk of coronary disease had decreased by 17 percent in the treatment communities, whereas it increased by more than 6 percent in the control community. Knowledge of risk factors increased proportionately with the intensity of the instruction and was highly correlated with improvement in "harmful" behavior, a composite of smoking and dietary intake of saturated fat and cholesterol.

Figure 6 shows the progression of improvement in the treatment groups compared with the lack of change in the control community. The high-risk subjects who received face-to-face instruction showed a remarkable 30 percent decrease in risk factors during the 1st year of treatment, compared with a lesser, but still statistically significant, decrease among persons receiving only the media program. By the end of the 2d year, however, the media-only treatments had produced a continuing rapid decrease in risk factors; the rate of decrease among the high-risk subjects having leveled off, the difference between the two groups was no longer statistically significant.

The magnitude of the effects of this study is suggested by the fact that a 30-percent reduction in the risk factors studied (the Cornfield risk factors) is equivalent to a 5-year increase in life expectancy. Such an increase is unprecedented in this kind of relatively large-scale intervention effort, and compares favorably with the 4-year increase in life expectancy at age 40 that has been the fruit of all our medical efforts between the years 1900 and 1970.

FIGURE 6.--Percent change from baseline (0) in risk of coronary heart disease after 1 and 2 years of health education in various study groups from three communities. Cardiovascular risk is measured by a multiple logistic function of risk factors.



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Clearly, major health benefits can be achieved with this kind of ambitious campaign. Its costs, however, are high. Can comparable results be reached through other, less costly, more effective means? The prospects are good. Many promising possibilities exist; even if no more than a few are realized, those few could transform the American health scene.

The Many Potential Influences of the Future

Very recent developments make it clear that leadership in broad-scale efforts to control obesity is passing to nonmedical agencies. As we look to the future, it appears that this trend may accelerate; the most promising new methods for controlling obesity seem to lie almost entirely outside the province of the medical profession. For obesity is, in large part, a result of the way we live; and the most effective means for controlling obesity today may lie in altering our lifestyles. Such an undertaking as changing the habit patterns of a nation is far beyond the capability of a profession like medicine; the social and economic forces that gave rise to those lifestyles and that sustain them must change.

These forces are powerful indeed. Consider just the impact on our nutritional practices of the amount spent on advertising each year by the food industry--$1.2 billion. Efforts by physicians to treat individual patients on a one-by-one basis are puny in comparison. They might be likened to exhortations to a swimmer to persevere against a raging current.

But what are the possibilities of swimming with the current? Changing the social and economic forces that maintain our lifestyles is not as overwhelming a task as it might at first appear. In the first place, relatively small changes in each of these could, by their cumulative--and perhaps potentiating--effects, bring about considerably larger changes. Second, these forces are not simply blind, economic ones; they involve human beings in positions of responsibility who can make choices between alternatives. Within their constraints, people generally choose what helps over what hurts. Finally, there is the possibility of generating powerful new social forces that can change the existing pattern. Public interest in personal health can be precisely this kind of force.

Just as the Nation has in the past taken special interest in particular afflictions--poliomyelitis and mental retardation, for example--so in the future it may well take an increased interest in general health, especially as it bears on prevention of illness. Obesity seems likely to be a prominent focus of any such interest. The recent "Perspective on the Health of Canadians" (101) and the subsequent activities of the Long-Range Planning Committee of the Canadian Department of Health and Welfare[1] illustrate how many different agencies might be mobilized to improve health and prevent illness. Consider first the possible contributions of the business world.

Industry

The leadership in the control of obesity currently exercised by industry depends largely upon one type of activity: direct service to clients. But such direct service is only one of five approaches that seem ideally suited to possible efforts by businesses to research and develop actions and policies that would help control obesity. The other four are: development of new food products for weight control; changes in the delivery of food through restaurants and catering services; provision of more opportunities for exercise through health clubs, health spas, and sporting goods manufacturers; and finally, insurance incentives for weight loss. Each of these five approaches can be effective as a freestanding enterprise; integration of various combinations of them could multiply this effectiveness.

- Direct service to clients. We have considered at some length the rise of commercial programs of direct service to clients, and this area needs no elaboration. Clearly established trends seem to ensure a strong, continuing role for commercial endeavors: the research-based increase in the efficacy of behavioral measures, the feasibility of their application by persons with progressively fewer educational qualifications, and the growing acceptance of nonmedical agencies.

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[1] T. Boudreau, personal communication, 1976.

TABLE 2.--Industry

Service delivery (clinical)
Product development
Delivery systems--restaurants
Delivery systems--health clubs and spas
Insurance incentives

- Development of new food products. One of the first and perhaps the most notable of the foods developed for weight reduction purposes was Metrecal, adapted from the "Rockefeller diet" of the mid-1950's. Metrecal was taken up by the public with an enthusiasm that astonished its pharmaceutical manufacturer; it quickly broke all kinds of sales records before its poorly understood, inexorable decline. Diet foods have become increasingly popular since the introduction of Metrecal, and Weight Watchers in particular has capitalized on this interest to sponsor a variety of franchised diet foods, quite independent of its program of lectures. Low-calorie beverages have occupied a large part of the soft drink market. But the potential for developing new products for weight control still seems virtually unlimited.
- The restaurant and food service industries. Despite the widespread concern with body weight on the part of vast numbers of persons who eat out, it is usually awkward or impossible to secure satisfying low-calorie, nonatherogenic foods in restaurants. Even when restaurants serve low-calorie dishes, all too frequently the choice is limited and the selection uninspired. There is great need for restaurants that serve an assortment of attractively prepared low-calorie dishes. This need could be met either through the establishment of specialty restaurants or by modifying some items on the menus of traditional restaurants.

Specialty (health) restaurants need not be explicitly identified with programs of direct service to clients. Such identification might limit the number and diversity of their customers, and they could serve a vital function for both members and nonmembers of client-service programs. Imaginative promotion of these restaurants, capitalizing on the Nation's growing interest in nutrition and health, could give birth to a vital new industry.

Modifying the menus of traditional restaurants could have an even greater impact on the nutrition of the American people than would the development of specialty restaurants, since traditional restaurants will presumably always attract vastly greater numbers of customers. Therefore, even small improvements in their offerings could affect the eating habits of tens of millions of persons. Such improvements could begin on a modest basis, involving no more than two or three items, thus permitting restaurants to explore the potential market before making a major commitment. If this exploration were to show that specially prepared items bring in at least as much profit as traditional dishes, it would not take long for business, in its own self-interest, to enlist in the campaign for improved nutrition. One pilot study has already produced encouraging results. A small restaurant chain in Houston, Texas, has begun to list on its menu the calorie content of a few items selected for their limited fat and calories and prepared with polyunsaturated oils. The first response was an increase in consumption of these items sufficiently promising to induce the company both to expand their number and to introduce a special menu to describe them.

The growth of large catering agencies that furnish complete food services for schools, businesses, and other institutions provides an important strategic opportunity for nutritional intervention. Increasingly large numbers of young people eat in facilities served by these agencies, and the nutritional education they receive in the process doubtless carries over to meals eaten elsewhere and to their future eating practices. Any improvement in the nutritional quality of the foods provided by these agencies would thus benefit vast numbers of people both now and in the future. Such improvement need not await the uncertain outcome of efforts to build a market in the highly competitive restaurant business; it could flow directly from management decisions involving a small number of experts in the relevant disciplines.

- Health clubs and spas. These businesses have already demonstrated their appeal to a large and growing market, even as freestanding enterprises. They, in particular, might be more effective and less costly as part of an integrated network of weight reduction agencies that also included restaurants for eating out, food products for eating at home, and nutrition/behavioral programs of direct service to clients. Enlisting the sporting goods industry in such enterprises is an unexplored area of potential effectiveness.

- Insurance. The greatest potential for changing health behavior through efforts by business may lie in an almost totally unexplored field. Assessment of the risk of death and disability lies at the heart of the insurance industry, which has achieved remarkable accuracy in predicting such outcomes for population groups and in modifying its predictions on the basis of changing health conditions. However, it has rarely attempted to alter these conditions. Unparalleled promise for the future may lie in that direction. The insurance companies may well possess the most powerful incentives for health behavior change in our society today.

Automobile insurance provides an instructive example. Premiums for young persons are routinely reduced solely on the basis of attendance at driver education courses, with no requirement for demonstrated effectiveness of this education in the case of the individual driver. The experience of population groups is sufficient insurance. Surely health education programs can be as sound actuarially. Reducing premiums for individuals contingent upon concrete evidence of health behavior changes such as reductions in weight or blood pressure would provide a powerful new incentive that can hardly be overestimated. Recent research on contingency contracting has shown that, for reasons not entirely clear, the symbolic value of relatively small rebates can be very great. And the potency of such rebates can be further increased through the imaginative use of incentives from other areas of industry. Membership in a health club or reduced rates for a vacation at a health spa could not only reward people for improved health behavior; the rewards themselves could become stimuli for further improvement.

Almost alone among the agencies of our society, the insurance industry benefits from improved prevention of disease. The change in life expectancy reported by the Stanford Three-Community Study (43), if achieved more widely, would have an enormous impact on the life insurance industry. The prospects of bringing about even a small part of that change could well warrant intensive efforts by life insurance companies. Similarly, health insurance programs could be immeasurably affected by simple preventive measures. Health insurance could have a more direct impact on health behavior than would life insurance--and an even stronger one, if that is possible. As health insurance programs become more closely associated with the providers of medical care, particularly through health maintenance organizations, they can furnish a powerful stimulus for the introduction of health behavior programs into medical care settings. In fact, this stimulus alone could finally make health maintenance an integral part of medical care.

The Media

Although the media are properly viewed as a form of industry, their special characteristics entitle them to separate consideration. The results of the Stanford Three-Community Study show the potential of an integrated mass media campaign. Such integration might be more difficult to achieve on a national or even regional basis, but any such disadvantages would be more than offset by the economy of scale and the relatively low cost, once the initial materials have been developed. Furthermore, we can expect continuing improvement in the capacity of the media, particularly of live and videotape television, to influence health behavior.

The media derive much of their power from their ability to influence all three factors of a behavior change program: knowledge, attitudes, and skills. Television is a shining example. Its ability to impart information is well established; suitably programed, it could educate the public about weight reduction, perhaps more effectively than any other method. Inducing changes in attitude is the second well-established capability of television; it has been particularly well exemplified by the success of advertising in changing attitudes toward commercial products. Measures to develop favorable attitudes toward health behavior--toward exercise and decreased food intake, for example--are well within the capability of the medium that has dictated American buying practices. Even small changes in the character of food advertising, with its $1.2 billion budget, could have a significant impact.

In contrast to the acknowledged capacity of television to inform and to change attitudes, it has generally been accepted that the development of skills is beyond the capabilities of the medium and that person-to-person interaction is necessary. However, the production of videotapes designed to show step-by-step procedures for behavior change has reversed this assessment and has brought training in health behavior skills--how to stop smoking, for example--within the range of anyone with access to a videotape viewer. Moreover, live television is being used increasingly to teach skills; a series on Los Angeles commerical television featured a step-by-step description of a weight loss program by an attractive newscaster who modeled the requisite behaviors while reporting her own progress in the program. An unofficial estimate suggested that residents of Los Angeles lost 700,000 pounds during the course of the program.

Education

An area that has long been neglected as a major source of weight control programs is the school system. Tens of millions of children are fed each day in our schools; their own nutrition as well as what they learn about nutrition is inexorably determined by public education policies. Yet nutritious hot school lunches are increasingly giving way to machine-dispensed "junk foods," with a resultant deterioration in both nutrition and nutrition education. Vigorous advocacy of improved nutrition and nutrition education by parent-teacher associations and school boards could reverse this trend and could have a major impact on childhood obesity and its pattern of stubborn persistence throughout adult life.

Failures of nutrition education do not stop at the elementary school level. The poor state of nutrition education in higher education, notably in medical schools, is undoubtedly one of the many factors contributing to the nutritional problems--including obesity--of our Nation.

Government

The potential of Government to play a role in the control of obesity has been realized as yet to only a limited degree. The taxing function, for instance, could be used as a powerful incentive to modify health behavior. Just as lowered insurance premiums might be offered for improvements in health behavior, so might tax rebates. Such a proposal seems fair. Our enormous medical costs are not generated equally throughout the population. Disproportionate costs are created by the excess illnesses of those who eat too much, drink too much, and exercise too little. It seems appropriate to build incentives for such persons to improve their health behavior by lightening their tax burden contingent upon loss of weight.

Government could also make a major impact by improving the nutrition of the millions of government employees it feeds every day--both in and out of the military. Improved nutrition could be coupled with nutrition education in each cafeteria and mess hall. Uncertainties over which foods constitute good nutrition have been resolved in part by the action of another arm of the Government--the report on Dietary Goals for the United States, prepared by the staff of the United States Senate Select Committee on Nutrition and Human Needs.

The Federal regulatory agencies have a long, distinguished history of service on behalf of the Nation's health. Years ago, Frances Kelsey's celebrated refusal to give Food and Drug Administration approval for the marketing of thalidomide spared this country the epidemic of malformed infants that afflicted our neighbors. More recently, the Federal Trade Commission's regulations requiring disclosure of nutritional content of packaged foods and its efforts to promote truth in advertising make it another major force in promoting nutrition education.

The climax of a vigorous, integrated governmental program of obesity control could be capped by the promotional capabilities of prominent government figures. Franklin Roosevelt, for example, helped to transform poliomyelitis from a fearsome plague to a national challenge. Here is power that can be exercised with remarkably little cost to remarkably great effect.

Worksite Training

A very promising opportunity for changing health behavior is the location of direct-service weight reduction programs at worksites. "On-the-job training" has a long and honorable history in American industry; on-the-job training to improve health behavior can be equally rewarding to worker and employer alike. Better health easily repays the costs of the program through improved work performance, decreased absenteeism, and, particularly, decreased hospitalization.

Fortunately, the potential of the worksite as a locus for long-term care has recently been demonstrated in a pilot project in a related area. Hypertension, like obesity, is rarely cured, but it does respond to adequate and available treatment. A large percentage of hypertensive persons, however, do not receive treatment, and those who do often receive inadequate therapy. Thus in a pilot project carried out under union auspices in New York City, less than half the hypertensives in conventional treatment had achieved satisfactory results. By contrast, the specially designed worksite program achieved long-term control of blood pressure in over 80 percent of the subjects and radically reduced the number of days of hospitalization for cardiovascular reasons. The health benefits and cost savings have been sufficiently encouraging to induce the union to expand services to 1,500 persons among 15,000 employees at 10 worksites.

Worksite programs have many advantages. First, time away from work is kept to a minimum--an hour a week for 20 weeks is sufficient for a serious program of weight reduction. Second, worksite programs obviate the high overhead costs of hospitals and the substantial, albeit lower, costs of rented space. Third, they greatly decrease the probability of missed appointments and treatment dropouts. A program carried out with the collaboration, and in part at the expense, of the employer exerts far stronger sanctions for attendance than one conducted during leisure time and with varying degrees of personal or family commitment. Fourth, jobsite programs tap potential for health behavior change heretofore unexplored in this country. Accounts from the People's Republic of China have given hints of how much can be achieved when concern for the health of individuals is complemented by concern for the health of working groups. Efforts to make unions and industries, or their subgroups, the focus of health behavior change programs can generate high morale and strong group participation. The organized support and encouragement of fellow workers can constitute an unprecedented stimulus for weight loss. Rewards given to groups for improving their collective health could be even more effective than those given to individuals. And these rewards might become even more effective as prizes for a competition between, for example, members of union locals for the number of excess pounds lost.

The potential clientele for jobsite health programs is enormous. Current executive and union health programs have no more than scratched the surface.

The vast numbers of persons in the employ of the Government--particularly those in the armed forces--provide attractive targets for health behavior intervention. The potential population is almost limitless.

Volunteer Agencies

Some religions inculcate an enviable series of health behaviors in their members and offer assistance to others trying to change their health behaviors. The Smoking Cessation Clinics conducted by the Seventh-Day Adventists are landmarks in such endeavors. It seems entirely reasonable to expect that, in a favorable climate, other health-promotion activities could be carried out under religious auspices. Weight control could qualify as a prime candidate.

TABLE 3.--Volunteer agencies

Religious: Seventh-Day Adventists, Mormons
Fraternal organizations: Lions, Shriners
Recreational organizations: YMCA, YWCA YMHA, YWHA
Volunteer health agencies: American Cancer Society, American Heart Association
Youth groups: Boy Scouts, Girl Scouts, 4-H Clubs, Future Farmers of America

Fraternal organizations have often taken a special interest in health care. The activities of the Lions on behalf of visually impaired children and of the Shriners on behalf of crippled children are notable examples. Other fraternal organizations might well develop an interest in other health problems, and an enlightened membership could decide to deal with its own health problems, such as overweight, as well as those of its beneficiaries.

Recreational organizations have traditionally taken a strong interest in health behavior. The gymnasiums of the Young Men's Christian Association, for example, are among the important health facilities of many communities. Encouraging the work of these organizations and facilitating their further efforts would capitalize on one of the traditional health-promoting agencies of our society.

Volunteer health agencies such as the American Cancer Society and the American Heart Association occupy a special place in the Nation's health care system. They have carried out extensive programs of health education, and the American Heart Association has already devoted some effort toward weight control. These agencies show great promise for disseminating new information about weight control and new techniques for achieving it.

Youth groups also have been a traditional source of health education and activity; the camps and outings of the Boy Scouts and Girl Scouts, for instance, have provided the major opportunities for physical activity for many boys and girls. Youth is a promising time of life, and youth groups offer promising vehicles for intensified efforts at preventing and treating obesity.

Permutations and Combinations

To this point we have been considering what might be called single-factor approaches to the control of obesity, but future approaches are not likely to be confined to such inefficient one-by-one forms of intervention. Combinations of different forms of intervention seem particularly promising. Combining interventions may in fact accomplish more than simply adding their effects; it may actually multiply them. We have discussed combinations that industry has taken in the past and could take in the future. The prospects of effectively integrating diverse strategies under commercial auspices seem bright. But such integration need not be confined to purely commercial ventures. Insurance carriers, for example, could require hospitals and health maintenance organizations to provide health education programs, including ones for obesity, as part of their contract. And if the insurance companies lagged in this enterprise, they could be encouraged toward greater efforts through judicious use of government regulations.

The volunteer agencies are in an excellent position to develop comprehensive programs of weight control. School-based programs could serve as a starting point. One or more volunteer health agencies could produce the syllabus and media materials, recruit volunteers for face-to-face teaching, and negotiate for time for weight-control programs on public or even commercial television. These agencies are well situated to enlist the President, movie stars, and famous athletes to increase the impact of the media messages, and to reward the achievements of both groups and individuals with low-cost symbols such as certificates, banners, and plaques. Once individual intervention strategies have been devised, the only limitations to their effectiveness would be those imposed by limitations on the creativity with which they are deployed.

In 1977 the Office of Health Information and Health Promotion, HEW, developed a matrix setting forth possibilities for individual and group action to improve nutrition and dietary practices, including the reduction of obesity (see the appendix).

Summary

Systematic studies have shown that social forces such as socioeconomic status exert a powerful influence on the prevalence of human obesity. This susceptibility of obese persons to social forces has been utilized by behavior modifiers to construct programs of obesity control that are more effective than traditional ones. These programs have recently been utilized successfully with large population groups in the first approach to the control of obesity that is sufficiently broad to warrant description as a public health measure. But this is only a beginning. A variety of agencies and institutions stand at the threshold of major new capabilities of controlling obesity. Industry is the most developed; no less than five different potential intervention strategies can be identified. But government, education, and numerous volunteer agencies are not far behind. Each could multiply its effectiveness by developing the enormous unused capabilities of the media for weight control. The prospects of worksite health training programs are almost entirely unexplored. Development of the capabilities of any of these agencies will contribute significantly to the control of obesity. Combining their capabilities in integrated programs of weight control could bring as yet unimagined benefits.

Appendix

Matrix for Action: Nutrition and Dietary Practices

Jane E. Fullarton

As mandated by Public Law 94-317, the National Consumer and Health Information and Health Promotion Act of 1976, the Office of Health Information and Health Promotion (OHIHP) was established in 1976 in the Office of the Assistant Secretary for Health, HEW. As one of its first priority areas, OHIHP selected nutrition, and during 1977 it developed a matrix of suggestions for improvement of nutrition and dietary practices, including the reduction of overweight and obesity, in the American population. The present matrix reflects the comments of many critics on previous versions.

Target Groups: Preschoolers (0 - 5 yrs) and their parents

In relation to both these target groups, all nutrition education efforts should have as their basis specific input obtained directly from the people concerning their needs/expectations which may then be related to the nutrition education needs as perceived by health care providers, media personnel, educators, industrial groups, the Government, and others.

Objectives for Preschoolers

1. Learn about good nutrition, its relationship to one's body and health.
2. Participate with parents and peers in making food choices that contribute to good nutrition.

Objectives for Parents

1. During prenatal period, adopt healthy dietary habits and relate these to the health of the child, as well as one's own personal health.
2. Practice healthy dietary habits in relation to infant and child feeding.
3. Teach young children about good nutrition, allow them to participate in choosing foods; where feasible, assisting in food preparation.

Home

1. Provide parents with nutrition education opportunities to learn about prenatal, infant, and child nutrition in the home environment, e.g., self-instructional materials, records, video discs, television programs, cable TV and two-way interactive communications, etc.
2. Enlist the help of community outreach workers, public health nurses, nutritionists, media personnel, and others to work with parents in arranging for educational opportunities in the home that will center on child nutrition.
3. Beyond the community outreach workers, enlist the help of parents in the community to organize "home nutrition education" efforts so that teaching might naturally occur among "parents-to-be" and for those with young children.
4. Encourage parents to have their young children assist them in choosing nutritious foods in the market, preparing and serving them.
5. Encourage parents to assist their children in using play time to "cook" foods for dolls, siblings, and other playmates relating good nutrition ideas to these situations.
6. Encourage parents to recognize the importance of normal weight maintenance in the infant and young child as this may have implications for weight gain in later life.

Community

1. Provide supermarkets and other grocery stores with self-assessment and child-assessment tools for distribution to parents so that they can determine their own nutritional health and that of their children; also distribute to the stores materials designed for young children, such as coloring books where they can color in the foods that are part of a nutritionally sound diet.
2. Involve these food markets in offering parents and young children nutrition education opportunities which might include matching demonstrations of food preparation by a nutritionist in the store or even by a lay member of the community, self-instructional or other materials they might take home, etc., to relate to the nutrition assessment in #1.
3. Encourage communities to assess the knowledge, attitudes, and nutrition habits of both parents and children, as well as the expressed needs of the parents, in relation to nutrition education as a basis for launching a total community-oriented nutrition education effort which could be developed and implemented with parent/child input.
4. Involve restaurants and other public eating places in promoting good nutrition through food selection available. Use of media advertising, including nutrition choices in distributed materials such as coloring books, comic books, and puzzles used as advertising by eating establishments.
5. Encourage churches to aid in the dissemination of nutrition knowledge through their adult education programs, newsletters, etc.

Schools

1. Encourage the staff of adult education programs, primary and secondary schools, community colleges, and universities to offer day/evening nutrition education courses and/or take-home course material focused on parent/child needs and nutrition information specifically geared toward the preschooler for his/her own learning.

2. Encourage PTAs to continue to work closely with those who plan and implement school lunch programs to assure their nutritional soundness.

3. Enlist the help of day care centers in incorporating nutrition-related learning experiences into their programs for children and preparing their staff to teach this topic, as well as serving nutritionally sound food to the children.

4. Enlist the help of schools and their health-related staff (school nurses, health educators, and teachers in general) in recognizing the special needs of children with metabolic disorders, referring to appropriate health care personnel, etc.

Media

1. Enlist the help of the media in working with nutritionists and other experts in the field to incorporate specific nutrition concepts into children's programing and develop innovative television programs where parents and children can interact together in selection of food in supermarkets, grocery stores (live on location), preparation of food at home, and serving at mealtime.

Worksite

1. Encourage employers to offer their employees, specifically "parents-to-be" and parents with children, nutrition instruction on the job through the traditional health units and/or more innovative approaches, such as the availability of nutrition education materials (print or nonprint) for parents related to infant and child nutrition in the cafeteria, coffee break areas, snack bars, lobby entrances, etc.

2. Encourage employers to work with fast food and other restaurants in their vicinity to provide their parent and child consumers with nutrition education materials, better choices of nutritious food on their menus, more information on their menus related to nutrition content, calories of foods, etc.

Government

1. Support research and demonstration efforts directed at the development of innovative nutrition curricula and material for both parents and children for use over current and newer communications systems, e.g., interactive TV, video discs, etc.

Target Groups: Preschoolers (0 - 5 yrs) and their parents

Media	Government
2. Enlist the help of the media in developing a series of nutrition-related cartoons which could be shown to children and their parents in toy stores, supermarkets, and public libraries.	2. Support community-organized demonstration projects in a variety of settings (communities where active citizen participation in community affairs is in place and other communities where this is not so; communities with different ethnic, socioeconomic makeup, etc.) to determine some alternative approaches to community nutrition education.
	3. Support research and demonstration in determining the most effective educational/behavioral and other interventions aimed at assisting youngsters and their families to adopt and maintain healthy nutrition habits (individualized learning packages to be used in any environment, including the home, school, health education curricula, specific self-care approaches, etc., based on their educational needs).
	4. Encourage the development of model preschool health education curricula with nutrition as an integral component and in a replicable format.
	5. Encourage governmental agencies to develop guidelines to be used by media, food manufacturers, distributors, and restaurants such that parents can make enlightened nutrition-related decisions for themselves and their children, a form of self-regulation and self-policing.
	6. Encourage the distribution of nutrition information along with food stamps for parents and their youngsters.

Private Sector

1. Enlist the help of food manufacturers and distributors to include with their food products educational opportunities for parents to learn more about good nutrition for their children and materials specifically designed for children, e.g., balloons, coloring/cutout books with fruits, vegetables, etc., on/in them.

2. Enlist the help of these same food companies in sponsoring nutrition education community courses for parents and their children.

3. Enlist the help of toy manufacturers to develop food-related toys that might be used to teach children about nutrition, e.g., cooking kits, food models, etc.

7. Support research and demonstration efforts to determine the most effective way of preparing nutritionists, dietitians, health educators, nurses, teachers, and others in the latest educational/behavioral techniques for assisting parents and youngsters to adopt healthy nutrition habits.

8. Require that day care centers and nurseries teach nutrition education and that only nutritious snacks and meals be served.

9. Support research and demonstration efforts to determine the most effective means of instruction to the public to assist them in adopting healthy nutrition habits.

Health Care System

1. Encourage health professionals, health care agencies, especially on State and local levels, to create more innovative health education programs, especially ones which permit outreach into the homes of clients such that nutrition education can be available to "parents-to-be," parents with youngsters, and the youngsters themselves.

2. Enlist the help of professional societies, educational institutions, and others in assuring that nutrition education is incorporated into the curricula of all health care professionals, with a special focus on prenatal, infant, and child nutrition.

3. Enlist the help of health care professionals to develop with health care consumers (in this case, parents and youngsters) community programs which could be based on consumer nutrition education needs.

Target Groups: Preschoolers (0 - 5 yrs)
and their parents

Private Sector

4. Enlist the help of the plant/flower industry to offer children an educational opportunity related to both plant and human nutrition when they acquire a plant, e.g., water, food, air, sunlight, (all contributing to plant and human health) conveyed in a picture booklet with the child given opportunities to feed and water the plant.

5. Encourage the creation of and/or expansion of community-based health activation of self-care efforts to include as a part of their total health program nutrition education for both "parents-to-be," parents with youngsters, and the youngsters themselves.

6. Encourage parents to work with restaurants (with possible emphasis on fast food places), industry representatives to encourage a better offering of nutritious foods in their restaurants, especially for children.

Health Care System

4. Encourage representatives from health care agencies on State and local levels, as well as self care and self help groups, to address the special needs of parents whose youngsters have metabolic disorders, through nutrition counseling, early detection, and treatment.

5. Encourage health care professionals to be alert to the signs and symptoms of malnutrition, iron deficiency, anemia, and other nutrition-related disorders, and to institute appropriate nutrition counseling accordingly.

6. Encourage dentists to teach parents about good dental health for children.

7. Encourage the support of insurance companies in covering the cost of preventive medical and dental care.

Target Groups: Youngsters (6 - 12 yrs)
and their parents

Objectives for Youngsters

1. Learn about good nutrition, its relationship to one's body and health status.

2. Participate with parents and peers in making food choices that contribute to good nutrition.

Home

1. Provide parents with nutrition education opportunities to learn about child nutrition in the home environment, e.g., self-instructional materials, records, video discs, television programs, cable TV, and two-way interactive communications, etc.

2. Enlist the help of community outreach workers, public health nurses, nutritionists and others to work with parents in arranging for educational opportunities in the home that will center on child nutrition.

Community

1. Enlist the help of supermarkets and other grocery stores in distributing to parents self-assessment and child-assessment tools they can complete to determine their own nutritional health and that of their children; also to distribute nutrition education materials designed for children, e.g., guides for selecting foods on the basis of nutrition labeling.

Objectives for Parents

1. Assist their children in adopting healthy nutrition habits.
2. Practice healthy nutrition habits themselves so as to serve as role models.

3. Beyond the community outreach workers, enlist the help of parents in the community to organize "home nutrition education" efforts so that teaching might naturally occur among parents with young children.
4. Encourage parents to have their young children assist them in choosing nutritious foods in the market, preparing and serving them.
5. Encourage parents to have their children participate with them in cooking foods for the family, relating good nutrition ideas to these situations.
6. Encourage parents to recognize the importance of normal weight maintenance in the child as this may have implications for weight gain in later life, as well as increasing their risk of certain diseases, such as heart, diabetes, etc.
7. Encourage parents to seek nutrition information from their children who have learned this in school.
8. Behavioral conditioning:
    a. avoid "clean plate habit"
    b. no TV, reading, etc., during meals
    c. no food reward/punishment
    d. eating slowly
    e. do not keep "junk foods" in home.

2. Involve these food markets in offering parents and children nutrition education opportunities which might include demonstrations of food preparation by a nutritionist, talks by nutritionists on nutrition labeling, menu planning, low-calorie food choices and preparation, etc., in the store or even by a trained lay member of the community, self-instructional or other materials they might take home, etc., to relate to the nutrition assessment in #1.
3. Encourage communities to assess the knowledge, attitudes, and nutrition habits of both parents and children, as well as the expressed needs of the parents, in relation to nutrition education as a basis for launching a total community-oriented nutrition education effort which could be developed and implemented with parent/child input.
4. Enlist the help of community organizations which focus on recreational needs of youngsters to offer the children who participate in these activities an opportunity to learn about nutrition education through outings, camp lunches, after-game cookouts, etc.
5. Encourage movie theater owners, ballpark concessionaires, etc., to make nutritious snacks available at concession stands—dried fruits, juices, crackers, fresh fruit, yogurt or Frogurt, etc.
6. Organize community nutrition week planned and implemented by citizens in cooperation with city government and local dietetic association.

Target Groups: Youngsters (6-12 yrs) and their parents

Schools

1. Encourage the staffs of adult education programs, primary and secondary schools, community colleges, and universities to offer day/evening nutrition education courses and/or take-home course material focused on parent/child needs and nutrition information specifically geared toward the child for his/her own learning.
2. Encourage PTAs to continue to work closely with those who plan and implement school lunch programs to assure their nutritional soundness. Also enlist the help of the PTAs in planning the nutritional component of the school curricula.
3. Make nutrition education a compulsory component of curricula.
4. Eliminate "junk foods" available in school snack bars, vending machines, and replace with nutritious, appealing alternatives.
5. Post nutrition education signs in school buses.
6. Include behavior modification techniques in school-sponsored nutrition education.

Worksite

1. Encourage employers to offer their employees, specifically those with children, nutrition instruction on the job through the traditional health units and/or more innovative approaches, such as the availability of nutrition education materials related to child nutrition (print and nonprint) in the cafeterias and snack bars.
2. Encourage employers to work with fast food and other restaurants in their vicinity to provide their parent and child consumers with nutrition education materials, better choices of nutritious food on their menus, more information on their menus related to nutrition content, calories of foods, etc.
3. Employer-sponsored nutrition workshops and seminars.
4. Provide employees with wise lunch/snack options in vending machines, snack bars, employee cafeterias.

Media	Government
1. Enlist the help of the media in working with nutritionists and other experts in the field to incorporate specific nutrition concepts into commercials and children's programing to counter poor nutrition habits encouraged by current advertising practices, and develop innovative television programs where parents and children can interact together in selection of food in supermarkets, grocery stores (live on location), preparation of food at home and serving at mealtime.	1. Support research and demonstration efforts directed at the development of innovative nutrition curricula and materials for both parents and children for use over current and newer communications systems, e.g., interactive TV, video discs, etc.
2. Enlist the help of the media in developing a series of nutrition-related cartoons, film clips, etc., which could be shown to children and their parents in toy stores, supermarkets, public libraries, and on TV.	2. Support community-organized demonstration projects in a variety of settings (communities where active citizen participation in community affairs is in place and other communities where this is not so, communities with different ethnic, socioeconomic makeup, etc.) to determine some alternative approaches to community nutrition education.
3. Extend first concept to all types of media--magazine ads, radio announcements, newspaper articles and ads, movie shorts, etc.	3. Support research and demonstration in determining the most effective educational/behavioral and other interventions aimed at assisting youngsters and their families to adopt and maintain healthy nutrition habits (individualized learning packages to be used in any environment, including the home, school, health education curricula, specific self-care approaches, studies of peer teaching/support in adopting/changing dietary habits, achieving and maintaining weight loss).
	4. Encourage the development of model school health education curricula with nutrition as an integral component and in a replicable format.
	5. Encourage governmental agencies to develop guidelines to be used by media, food manufacturers, and distributors such that parents can make enlightened nutrition-related decisions for themselves and their children, a form of self-regulation and self-policing.

Target Groups: Youngsters (6–12 yrs)
and their parents

Private Sector

1. Enlist the help of food manufacturers and distributors to include with their food products educational opportunities for parents to learn more about good nutrition for their children and materials specifically designed for children, e.g., balloons, coloring/cutout books with fruits, vegetables, etc., on/in them.
2. Enlist the help of these same food companies in sponsoring nutrition education community courses for parents and their children.
3. Enlist the help of toy manufacturers to develop food-related toys that might be

Government

6. Encourage the distribution of nutrition information along with food stamps for parents and their youngsters.
7. Support research and demonstration efforts to determine the most effective way of preparing nutritionists, dietitians, health educators, nurses, teachers, and others in the latest educational/behavioral techniques for assisting parents and youngsters to adopt healthy nutrition habits.

Health Care System

1. Encourage health professionals, health care agencies, especially on State and local levels, to create more innovative health education programs, especially ones which permit outreach into the homes of clients such that nutrition education can be available to "parents-to-be," parents with youngsters, and the youngsters themselves.
2. Enlist the help of professional societies, educational institutions, and others in assuring that nutrition education is incorporated into the curricula of all health care professionals, with a special focus on prenatal, infant, and child nutrition.

used to teach children about nutrition, e.g., cooking kits, food models, etc.

4. Enlist the help of the plant/flower industry to offer children an educational opportunity related to both plant and human nutrition when they acquire a plant, e.g., water, food, air, sunlight (all contributing to plant and human health), conveyed in a picture booklet with the child given opportunities to feed and water the plant.

5. Encourage the creation of and/or expansion of community-based health activation or self-care efforts to include, as a part of their total health program, nutrition education for both "parents-to-be," parents with youngsters, and the youngsters themselves.

6. Encourage parents to work with fast food industry representatives to encourage a better offering of nutritious foods in their restaurants, especially for children.

7. Nutrition information on cereal boxes.

8. Develop nutritious, low-fat, low-sugar snack foods.

9. Food industry should use polyunsaturated fats in processed foods.

10. Meat industry should produce low-fat meats with higher percent polyunsaturated fat content.

3. Enlist the help of health care professionals to develop with health care consumers (in this case, parents and youngsters) community programs which could be based on consumer nutrition education needs.

4. Encourage representatives from health care agencies on State and local levels, as well as self-care and self-help groups, to address the special needs of parents whose youngsters have metabolic disorders, through nutrition counseling, early detection, and treatment.

5. Encourage health care professionals to be alert to the signs and symptoms of malnutrition, iron deficiency, anemia, and other nutrition-related disorders, and to institute appropriate nutrition counseling accordingly.

Target Groups: Teenagers (13 - 20 yrs)
and their parents

Objectives for Teenagers

1. Adopt and maintain healthy dietary habits.
2. Identify those dietary habits not conducive to good nutrition and alter these as necessary.
3. Maintain weight at appropriate levels, and reduce weight when necessary to achieve a healthier status.

Objectives for Parents

1. Encourage teenagers to take responsibility themselves for maintaining healthy dietary habits and weight levels.
2. Adopt and maintain healthy dietary habits and weight levels so as to serve as good role models.

Home

1. Encourage parents to have their teenage children develop meal plans for the family, as well as prepare the food in a manner that is conducive to good nutrition.
2. Provide teenagers in the home environment with educational opportunities related to good nutrition using a variety of print and nonprint media, e.g., self-instructional packages, TV, video discs, cable TV, etc.
3. Encourage parents and teenagers to work together in seeing that nutritious snacks are available for those teenagers who eat between meals.
4. Teach parents, school teachers, and health workers how to check nutritional adequacy of food records.
5. Help families to understand that there are also barriers to good nutrition other than lack of knowledge, i.e., time management, attitudes toward food, role models, emotional problems, lifestyle characteristics, money management, heredity, superstition, and rebellion; and teach them to overcome these barriers.
6. Encourage good eating behavior habits and use of behavior modification.

Community

1. Enlist the help of social, religious, and related community organizations with a large teenage membership in designing activities with those teenagers that will provide nutrition-related learning experiences for them when structured properly, e.g., assisting elderly members of the community in selection and preparation of foods, having picnics for peers or younger children.
2. Enlist the help of supermarkets and other grocery chains in developing innovative exhibits in their stores where teenagers can ask and obtain answers to nutrition questions.
3. Encourage community organizations to hold open forums on nutrition and food misinformation with teenagers involved in the panels along with experts such as nutritionists and others.
4. Promote health fairs for teenagers involving many health care agencies providing information related to nutritional needs.
5. Enlist help of agencies or community groups with large teenage membership to conduct cooking classes for teenagers. Highlight specific problem areas:
   a. preparing quick breakfasts
   b. preparing nutritious snacks.
6. Encourage local parks and recreation departments to sponsor physical fitness and weight control programs for youth.

Schools

1. Involve the schools in working closely with fast food chains and other food stores in efforts to provide teenagers with appropriate nutrition information such that they will be able to make better informed food choices.

2. Encourage schools to have teenagers develop the nutrition component and related field experiences in the school health education curricula.

3. Encourage schools to enlist the help of teenagers in teaching each other and their parents about good nutrition.

4. Encourage schools to incorporate into their health education curricula educational strategies to assist teenagers and their parents to select from a fast food menu, foods that when combined, will provide greater nutritional adequacy.

5. Involve schools in education about food ingredients to encourage students to read labels and become acquainted with those ingredients which are nutritious and those which are not.

6. Encourage local school food service directors to establish innovative nutrition education programs involving cafeteria workers and students. Use Type A lunches as educational tool for teaching good nutrition.

7. Encourage school personnel to eliminate "empty calorie" food vending machines and replace with nutritious foods in vending machines.

Worksite

1. Enlist the help of industry in developing health education programs with a nutrition component that address the specific needs of teenagers and are developed with them.

2. Encourage employers to set up demonstration projects to involve teenagers in menu-planning at on-site cafeterias.

3. Encourage employers to have attractive and well-lighted company cafeterias creating an atmosphere more conducive to relaxed dining.

Target Groups: Teenagers (13-20 yrs) and their parents

Schools

8. Conduct animal studies in biology classes or health classes demonstrating effect of good diet vs. "junk food" diet.

9. Encourage fast food chains to provide salads or an alternative to fried foods.

10. Encourage the school food service to allow teenagers to assist in planning menus that include foods that will be eaten rather than thrown away.

Media

1. Encourage the help of the media in informing teenagers and their parents about current approaches to weight reduction, including some of the ill-advised diets, but in a manner which objectively outlines the positive and negative aspects, such that both the teenager and parent can make intelligent decisions regarding health actions to be taken.

2. Encourage the development of media which address the needs of teenagers, some of their special concerns, especially in the weight reduction area, and can be utilized in some of the newer communications systems: video discs, cable TV, satellites, etc.

3. Encourage the media to provide public service announcements geared toward the improvement of teenage nutrition with special attention to increasing awareness of food labeling and ingredients.

Government

1. Hold public hearings to encourage consumers, especially teenagers and their parents, to define their expectations and needs for nutrition information; also their concern in relation to the many conflicting nutrition messages they receive so that well-defined education programs can be formulated.

2. Support research and demonstration efforts to determine the most effective education and behavioral strategies for motivating teenagers to accept greater responsibility for maintaining healthy dietary habits (peer teaching and support interventions, behavioral contracting methods, self-instructional materials, etc.).

4. Develop PSA using popular figure teenager relates to, giving testimonial on importance of good nutrition in life, i.e., athlete, football player, popular singer, tennis player, model, etc.

5. In public arenas where instant replay screens are available, develop nutrition spots.

6. Encourage "rock" radio stations to play nutrition spots.

Private Sector

1. Enlist the help of food manufacturers and distributors to include with their products educational opportunities for parents to learn more about good nutrition for their children and materials specifically designed for children, e.g., kites in the form of fruits, vegetables, with information booklets, etc.

2. Enlist the help of these same food companies in sponsoring nutrition education community courses for parents and their children.

3. Encourage private companies and utility companies to conduct cooking clinics for teenagers.

4. Sponsor seminars, panel discussions, tasting parties on nutritional needs of teenagers.
    a. conduct good grooming courses incorporating principle of good nutrition with beauty and weight control
    b. conduct physical fitness programs

Health Care System

1. Encourage health professionals, health care agencies, especially on State and local levels, to create more innovative health education programs, especially ones which permit outreach into the homes of clients such that nutrition education can be available to parents with youngsters, and youngsters themselves.

2. Enlist the help of professional societies, educational institutions, and others in assuring that nutrition education is incorporated into the curricula of all health care professionals, with a special focus on child nutrition.

3. Encourage health care industry to educate public in the area of proper nutrition as it pertains to healing and to maintaining good health.

4. Encourage representatives from health care agencies on State and local levels, as well as self-care and self-help groups, to address the special needs of parents whose youngsters have metabolic disorders, through nutrition counseling, early detection, and treatment.

Target Groups: Teenagers (13-20 yrs) and their parents

Private Sector

c. donate money for building tennis courts, swimming pools, exercise rooms, etc., summer camps, staffed with qualified people to teach physical fitness as well as provide nutritional information for teenagers.

5. Encourage private companies to develop and promote more nutritious snack foods.

6. Encourage parents to work with fast food industry representatives to encourage a better offering of nutritious foods in their restaurants, especially for children.

Health Care System

5. Encourage health care professionals to be alert to the signs and symptoms of malnutrition, iron deficiency, anemia, and other nutrition-related disorders, and to institute appropriate nutrition counseling accordingly.

6. Support the evaluation of some of the more innovative school health education curricula where nutrition is an integral component.

7. Encourage the distribution of nutrition information along with food stamps for parents and their youngsters.

8. Support research and demonstration efforts to determine the most effective way of preparing nutritionists, dietitians, health educators, nurses, teachers, and others in the latest educational/behavioral techniques for assisting parents and youngsters to adopt healthy nutrition habits.

9. Support the development of models to involve the parents (e.g., PTAs, community action groups) in the development of school health education curricula of which nutrition is a component and to find ways of teaching the parents about nutrition to effect change in their dietary habits and those of their children.

10. Encourage accurate labeling on food products, showing all ingredients and nutritional information.

Target Group: Adults (21 - 65 yrs)

Objectives

1. Adopt and maintain healthy dietary habits.
2. Reduce and maintain weight reduction over time where indicated.

Home

1. Education of parents if possible, since they select and prepare foods for family.
2. Encourage family to use good food habits, such as eating as a unit at the table, not in front of the TV.
3. Encourage weighing and exercising daily as a family unit.
4. Discourage the "clean plate" system.

Schools

1. Fund the development of a series of innovative curricula in teaching nutrition and weight control to youngsters and their families, which could be part of a demonstration project.
2. Enlist the help of the schools to show the video tapes developed (under Media #2) by the media during school lunch hours, physical education and/or health education classes.
3. Enlist the help of schools to offer evening classes to youngsters, their parents, and other adults in community on how to prepare attractive and nutritious dietary plans as well as low-calorie ones.
4. Improve school lunches by redirecting emphasis of menus to low-calorie, low-cholesterol foods.

Community

1. Promote wider advertisement and use of Dial-A-Dietitian programs.
2. Publication and distribution of low-calorie and low-cholesterol shopping lists in grocery stores.
3. Use of behavior modification techniques, i.e., shopping from a list.
4. Encourage grocery stores to hire dietitians to present educational programs, introduce low-calorie, low-cholesterol foods, and give cooking demonstrations in stores to educate public.

Worksite

1. Fund demonstration projects at the work site aimed at involving individuals in adoption and maintenance of healthy dietary habits and at the prevention and control of obesity in particular.
2. Enlist the help of employers in showing their employees the video tapes developed (under Media #2) by the media during the lunch hours and/or regular work schedule.
3. Propose to develop with industry and the States guidelines for State programs of weight control.

Target Group: Adults (21-65 yrs)

Schools

5. Remove "junk foods" from vending machines and replace with nutritious alternates, such as fresh fruit or fruit juices.

Media

1. Enlist the help of media gatekeepers in introducing healthy dietary habits with current programing, especially soap operas, cartoons, and have these available for the time slots when the appropriate target groups (age, sex, etc.) can view them.
2. Enlist the help of the media in producing a series of video tapes which offer not only information related to exercise and food nutrition but proven, effective techniques for adopting and maintaining dietary habits including weight reduction and which address the needs of specific age, socioeconomic, and ethnic groups.
3. Initiate nutrition education programs on radio and television.
4. Place nutrition information spots on buses, subways, etc.

Government

1. Propose that any national health insurance program that is established recognize obesity as a disease and include within its benefits coverage for the treatment of it.
2. Enlist the help of the USDA to continue the nutrition education of home economists, nutritionists, dietitians, and others responsible for preparation of school lunch programs with a deliberate attempt to involve the parents of the children.
3. Support research in the development of palatable, low-calorie food products and make such findings readily available to food manufacturers and distributors.
4. Disseminate information or effective intervention related to health promotion/prevention and education.
5. Support research in determining the most effective educational/behavioral and other interventions in assisting youngsters and their families to adopt and maintain healthy dietary habits.

Private Sector

1. Propose that the insurance industry develop nutrition-related incentives for reducing the cost of life insurance premiums.

2. Educate restaurant and food industry personnel on how to better prepare attractive, palatable, low-calorie foods.

3. Enlist the help of the American Dietetic Association in working with pharmacists and dentists to distribute educational materials on nutrition to their customers and patients.

6. Support the development of programing for two-way interactive and other communications systems whereby individuals can assess their own health status related to nutrition, weight control, and exercise habits, etc.; develop for themselves with the aid of educational/behavioral techniques, a health behavior plan to reduce their risk of certain diseases; implement that plan, and return to the communication system to reassess their status, adjust their plan, and obtain continued emotional support.

7. Propose a "National Nutrition Week" to inform people about the relation of nutrition and health.

8. Make nutrition counseling reimbursable under Medicare.

9. For commodities to the school lunch program, provide only foods low in cholesterol and saturated fat.

Health Care System

1. Enlist the help of professional societies and institutions having programs to prepare health care providers (doctors, nurses, nutritionists, etc.) in efforts to include in basic and continuing education programs information related to assisting well and ill individuals to adopt and maintain healthy dietary habits.

2. Enlist the help of health care providers in the health care system to provide as a matter of routine, instruction and assistance to well and ill individuals (regardless of their health status) regarding the adoption and maintenance of health dietary habits.

Target Group: Adults (21-65 yrs)

Private Sector

4. Enlist the help of health clubs, spas, nutritional/behavioral programs in clinics and private organizations, church groups, etc., to coordinate all of their nutrition/weight reduction activities so as to provide the instructive/supportive links needed by individuals to maintain nutrition behavior changes over time.

5. Enlist the help of travel companies and health spas to promote reduced rates for vacations to health spas where adequate instruction and care related to good dietary habits/weight reduction, etc., can be offered. In addition, enlist the help of these groups in providing some linkage with the medical and community support systems from which the participating individuals come to promote continuity of care and followup.

6. Enlist the help of airline companies, restaurants, and others to inform the public about the caloric content of meals.

7. Encourage restaurants to offer choices of food portion sizes to customers.

8. Enlist the help of industry to make available to more homes two-way interactive and other communications facilities such that instruction related to nutrition might be readily available to individuals in their homes.

9. Make payments for nutrition counseling, and for smoking and exercise program reimbursable.

10. Encourage grocery stores to change marketing strategies to emphasize nutrition rather than impulse buying.
11. Encourage manufacturers to develop food products low in saturated fat, high in polyunsaturated fat, and low in cholesterol.

Target Group: Individuals over age 65

Objectives

1. Recognize the strengths and weaknesses of present dietary habits and the need to maintain or alter one's weight level.
2. Adopt and maintain dietary habits conducive to good nutritional status and appropriate weight levels.

Home

1. Encourage individuals over 65, especially those living alone, to identify activities which they might like to participate in with their peers living nearby that could involve the preparation of nutritious food and eating together, e.g., in each others' homes, picnics, etc.
2. Encourage individuals over 65 living in housing which provides cable TV to participate in making video tapes such that they give demonstrations of ways to prepare food, discussions of the problems of cooking when alone, shopping for food when transportation to and from the store is lacking or difficult, etc. These tapes could be viewed by others in the same housing complex.
3. Encourage individuals over 65 to partake of "meals on wheels" and transportation services to and from food chains.
4. Enlist the help of specific individuals over 65 who have an interest in or may already be visiting the homes of neighbors/friends to assist them in cooking or even shopping for food to continue these services and learn more about the selection/preparation of nutritious foods.

Community

1. Enlist the help of community organizations, self-help groups, self-care programs to coordinate their efforts such that individuals over 65 are taught how to take care of their nutritional needs at home.
2. Enlist the help of church, social, civic, and recreational organizations in identifying individuals over 65 in their community in need of help with their nutrition practices and see that nutrition counseling is provided them.
3. Design "grocery store on wheels." Outfit large vans as grocery stores so quality foods at fair prices can be provided to the inner city elderly.
4. Provide greater protection for elderly so they feel safe on streets en route to grocery store.
5. Encourage churches to establish lunch programs for elderly in that elderly either bring covered dish to church for lunch or prepare lunch in church facilities.
6. Provide transportation to any program under discussion.
7. Establish outreach offices to find elderly in need and determine their immediate needs.

Target Group: Individuals over age 65

Schools

1. Encourage the schools to hold classes free of charge, preferably in the day-time, for individuals over 65 that would teach them about good nutrition, weight maintenance, etc.

2. Encourage the schools to provide youngsters who have learned about good nutrition an opportunity to teach this to individuals in the community over 65, e.g., class field trips to nursing homes where teenagers and senior citizens work together to make meals--benefiting both groups.

Media

1. Encourage the media to develop special programs which focus on the nutrition needs of individuals over 65, include them on the programs, and demonstrate ways in which individuals over 65 can help themselves and others with their dietary habits.

2. Encourage the development of special media for individuals over 65 which depend to a great extent on visuals, large print, and audio tracks that can be individually adjusted for loudness to convey nutrition messages to individuals over 65.

Community

8. Coordinate all efforts in community.

Worksite

1. Enlist the help of employers in providing special classes for families of individuals over 65 such that they can become better acquainted with the specific nutrition needs of this age group and learn ways in which they can help their parents and other relatives in adopting and maintaining healthful dietary practices.

2. Encourage employers to include sample menus and nutritional information with paychecks or strategically locate such "giveaways" throughout the worksite.

Government

1. Support the evaluation of some of the more innovative self-care programs and other related activities which are attempting to help individuals over 65 to be self sufficient in taking care of their own health needs, especially nutritional ones, at home.

2. Support research and demonstration efforts aimed at determining the most effective educational and behavioral strategies for assisting individuals over 65 to adopt and maintain healthy dietary habits and weight levels.

3. Encourage newspapers to print articles on nutritional needs of elderly. Food sections devote columns to food needs of elderly.	3. Support the development and evaluation of specific nutrition education materials which can be utilized over a variety of communications media, TV, cable TV, etc., and reach individuals over 65 in their homes.
	4. For those on fixed incomes who may not qualify for food stamps, provide some alternative means of supplementing the nutritional intake of individuals over 65; also provide these individuals, as well as those on welfare and/or getting food stamps with sound nutrition information via booklets or other means.
	5. Support research and demonstration projects to determine the factors that influence poor dietary habits in individuals over 65 and strategies (peer counseling, increasing socialization) that might be employed (based on these factors) to increase good nutritional practices among this age group.
	6. Support food and nutrition programs for individuals over 65 which would encompass not only food assistance and group meals in a social setting, but also include: a. adequate transportation for food shopping and to group meals; b. home-delivered meals; c. comprehensive ongoing activities directed at identifying and providing services to individuals over 65 who are in need of help with their nutritional practices; d. investigate local feeding programs to ensure nutrition education incorporated into total program; e. provide modified meals at feeding sites.

Target Group: Individuals over age 65

Private Sector	Health Care System
1. Encourage supermarkets, grocery stores, etc., to provide individuals over 65 with educational materials related to the nutritional needs of this age group.	1. Enlist the help of nursing homes in involving nutritionists/dietitians in the supervision of food preparation for the patients in those facilities.
2. Encourage food manufacturers and distributors to develop nutritional food packages that can be easily prepared, yet will meet the needs of an individual eating alone.	2. Enlist the help of hospitals and other health care facilities in setting up demonstration outreach programs that would provide adequate followup care for those individuals over 65 discharged to their homes.
3. Encourage self-help groups dealing specifically with the needs of the elderly to identify the services they provide, especially any that relate to nutrition, in an attempt to share some good approaches, possibly expand their services to include nutrition if this is not already being done, and to evaluate some of their strategies.	3. Encourage health care agencies, professional societies, and educational institutions involved in the preparation and continuing education of physicians, nurses, dentists, nutritionists, health educators, and others to include in their respective curricula theory and learning experiences that specifically address the nutrition needs of individuals over 65.
4. Encourage restaurants and cafeterias to provide special prices to senior citizens during non-peak hours to make available meals that individuals over 65 would be unlikely to cook for themselves.	
5. Present food demonstrations and/or cooking clinics in cooperation with utility company home economists, showing how to prepare simple meals for elderly.	
6. Encourage supermarkets to make available in their stores community resource people (dietitians) to answer questions of elderly and promote easy-to-prepare nutritional dishes.	
7. Encourage food companies to develop more nutritionally balanced TV dinners.	

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INDEX

Acupuncture, 202
Adenosine triphosphate, 60-61
Adipocytes, 23, 33, 85, 96
Adipomuscular ratio, 28
Adipose tissue
  cellular character, 79-81
  development, 84-87
  measurement of, 23, 24
  morphology, 78-81
  trapped calories, 63
American Cancer Society, 8, 238
Amino acids, 45
Amphetamines, 179-184
Amylase inhibitors, 189
Android fat, 22
Animal models
  adipose tissue development, 84-87
  metabolic studies
    adipose tissue and cells, 89-92
    dietary factors, 93-94
    muscle and liver, 93
  obesity development
    genetic factors, 88-89
    hypothalamic factors, 87-88
Anorectic agents
    amphetamines, 179-184
    L-Dopa, 184
    efficacy, 181-182
    gastrointestinal hormones, 184
    safety, 182-183
Aphagia syndrome, 38
Appetite suppressants.
    See Anorectic agents
Arthritis, 111, 199
Atherosclerosis, 115

BAY d 7791, 189
BAY e 4609, 189
Behavior therapy, 174-175, 214-222
Blood pressure
  related to age, race, sex, 30,31
  related to relative weight, 129, 130T, 131T
  related to skinfold measurement, 30
Body composition, 96-102
Body mass index, 5, 6T, 24
Brain serotonin.
  See 5 Hydroxytryptamine

British Medical Research Council, 25
Build and Blood Pressure Study of 1959, 24

Caloric intake, 11T
Calorigenic drugs
  growth hormone, 186
  thyroid hormones, 184-186
Cardiovascular risks, 112, 128, 138-140
Central receptors, 42-43
Cholecystokinin, 46, 184
Cholestyramine, 188-189

Decapeptide, 184
Deep obesity model, 105-107
Densitometry, 27
2-Deoxy-d-glucose, 47
"Diabesity," 32
Diabetes, 81-83, 109-111, 133
Dieting, hazards of
    diet pills 1
    protein supplements 2
Diets
  low-carbohydrate, 171
  low-calorie, 169-171
  protein, 168
Dilantin.
  See Diphenylhydantoin
Diphenylhydantoin, 192-193
L-Dopa, 184
Dopaminergic nigrostriatal pathway, 38

Eating
  hypothalamic control of, vi
Endometrial carcinoma, 114-115
Energy expenditure
  adenosine triphosphate, 60-61
  exercise, 53-58, 172-174
  respiratory quotient, 54-58
  thyroxine, 61-62
Trans-epoxyaconitic acid, 191
Exercise, 53-58, 172-174
Exogenous obesity, 31

Fasting, 164-169

Fat
  distribution of
    android, 22
    "cushingoid," 23
    gynecoid, 22
    in relation to muscle, 28
    measurement, 28-31
  measurement of
    densitometry, 27
    electromagnetic, 27
    skinfold, 25, 26T, 27
    whole-body plethysmography, 27
  percent by weight for age/sex, 95-96
Federal Trade Commission, 235
Feeding centers, 37-41
Food and Drug Administration, 168-169, 181
Food intake
  central receptors, 42
  dietary influence, 48
  environmental/social factors, 49-51
  glucostatic theory, 52
  hepatic influence, 46-48
  hormonal regulation, 46
  hypothalamic control, 37-41
  internal regulation, 51-52
  neural regulation, 44-45
  norepinephrine, 41-42
  nutrient regulation, 45-46
  peripheral receptors, 43-44
Food quotient, 55
Framingham Study, 34, 109, 125-163
Fructose, 47
Futile cycles 58-59

Gallbladder, 115-117
Gastric bypass
  complications, 201-202
  indications, 200
  mortality, 201
  results, 200-201
  theory, 199-200
  therapeutic failure, 201
Glucose, 46-47, 90-91, 93, 131-134
Glucose receptor blocking agents, 188
Glycerol, 51-52
Glycosuria, 132
Gout, 111, 134
Growth hormone, 186
Gynecoid fat, 22

HCG. See Human chorionic gonadotropin
Health and Nutrition Examination Survey (1971-74), 10, 29
Health clubs and spas, 231
Hormones
  growth hormone, 186
  human chorionic gonadotropin, 187
  progesterone, 192
  thyroxine, 185-186
  triiodothyronine, 185
5-HT. See 5-Hydroxytryptamine
Human chorionic gonadotropin, 187
Hydroxycitrate, 191-192
5-Hydroxytryptamine, 42
Hypercellular obesity, 79-80
Hypercholesterolemia, 83-84
Hyperinsulinemia, 82-83, 87
Hyperlipoproteinemia, 83
Hyperphagia, 38, 87
Hypertension, 107, 108T, 109
Hypertriglyceridemia, 23, 28
Hypertrophic obesity, 80
Hypothalamic obesity
  feeding syndromes, 38-41
  insulin secretion, 40
  lipostatic theory, 39
  metabolic correlates, 39-41
  motivational correlates, 40
  short-term satiety theory, 39
Hypothalamus, 37-39, 88
  central receptors, 42-43
  peripheral receptors, 43

Indomethacin, 187
Insulin, 81-83, 91-92
Insurance, 231-232
Intestinal bypass
  benefits, 195-196
  complications
    arthritis, 199
    bacterial overgrowth, 198
    diarrhea, 196
    liver disease, 197
    malnutrition, 196
    operative, 196
    renal failure, 198
    urinary calculi, 198
  indications, 193-194
  mechanism of weight loss, 194-195
  reanastomosis, 199

Jaw wiring, 203
Jejunoileostomy.
  See Intestinal bypass

Ketosis, 171

Lean body mass, 96, 98T
LH feeding syndrome, 38
Lipids, 129
Lipoprotein lipase, 87
Lipostatic theory, 39
Liver, 46-48

Media, 224, 232-233
Menstrual cycle, 112, 113T
Methylcellulose, 191
Metrecal, 229
Midtown Manhattan Study, 206-210
Minimal effective weight, 28
Mortality, 117, 118T, 140-141
Myocardial hypertrophy, 112

National Commission on Diabetes, 81
National Commission on Diabetes, Workgroup on Epidemiology, 32, 35
National Institutes of Health, Task Force for Hypertension, 35
National Obesity Registry, 122
Neomycin, 188
New food products, 229

Obesity
  adipocytes, 22, 33, 36
  and age, 3, 4, 210
  age of onset, 22, 23, 36
  animal models, 84, 86
  classification, 106, 106T, 107
    exogenous, 31
    hypercellular, 79-80
    hypertrophic, 80
  deep obesity model, 105-107
  definition, 2
    operational, 2
    social, 20
    statistical, 21
  dietary factors, 93-94
  environmental factors, 32
  estimation of 23, 24
  genetic factors, 32, 75, 88-89
Obesity(cont.)
  health hazards of, 8, 23, 74, 81, 103-124, 128-134, 138-143
  and income level, 3, 4, 207 208T, 212-214
  influence of behavior therapy, 214-222
  influence of group dynamics, 214-224
  influence of the private sector, 14, 17-18
  influence of the public sector, 14-17
  influence of volunteer agencies, 14, 18-19
  knowledge gaps, 10, 11, 14-16
  London Study, 209-210
  measurement of, 24, 25, 70, 136-137
  media campaigns, 224
  metabolic complications 81-84
  Midtown Manhattan Study, 206-210
  natural history, 72-74
  prevalence, 2-5, 34-36, 207, 208T
  psychological/social factors, 77, 117-120
  racial/ethnic factors, 76, 208
  and religious affiliation, 209
  research recommendations, 121-124
  and sex, 2, 3, 4
  and socioeconomic status, 35, 75-76, 207, 208T, 210-212
  therapeutic study, 203-205
  treatment. See Treatment
Operational obesity, 21
Ovaries, 112-114
Overweight
  definition of, 2

Perfluoroctyl bromide, 190
Peripheral receptors, 43
PFB. See Perfluoroctyl bromide
President's Council on Physical Fitness, 17

Reanastomosis, 199
Respiratory quotient, 54-58
Restaurants, 229-231

Self-help groups, 220-222
Senate Select Committee on
  Nutrition and Human Needs,
    120
Setpoint concept, 65-67
Seven Country Study, 34
Short-term satiety theory, 39
Skinfold fat measurement, 25,
  26T, 27, 28, 70-71, 97T
Social obesity, 20
SPE. SEE Sucrose polyester
Specific dynamic action, 62-63
Stanford Heart Disease
  Prevention Program, 175, 224
Statistical obesity, 21
Sucrose polyester, 190

TEAA. See Trans-epoxyaconitic
  acid
Ten State Nutrition Survey
  of 1968-70, 34
Thyroid hormones, 184-186
Thyroxine, 61-62, 185-186
TOPS (Take off Pounds
  Sensibly), 217, 220-222
Treatment
  acupuncture, 202
  adherence to regimes,
    176-178
  behavior therapy, 174-175
  community-based programs,
    175-176
  diets
    low-calorie, 169-171
    low-carbohydrate, 171
    protein, 168
  exercise, 172-174
  fasting, 164-169
  jaw wiring, 203
  pharmacologic
    anorectic agents,
      179-184
    calorigenic agents,
      184-186
    digestion/absorption
      blocking agents,
        188-191
    lipolytic agents, 187
Treatment
  metabolic blocking
    agents, 191-192
  predicting results of, 12
  surgical
    gastric bypass, 199-202
    intestinal bypass,
      193-199
Triglycerides, 25
  related to subscapular
    skinfold measurements, 29
Triiodothyronine, 185

Vagal nerve, 44, 48-49
VMH feeding syndrome, 38-41
Volunteer agencies, 237-238

Weight, 5
  changes with age, 134-136
  "ideal," 7T, 71, 127
  lipid levels, 129
  "minimal effective," 28
Weight control
  external/cognitive controls,
    67-68
  government influence,
    234-235
  influence of business and
    industry, 228-232
  influence of the media,
    232-233
  influence of the school
    system, 233-234
  programs
    TOPS (Take off Pounds
      Sensibly), 217, 220-222
    Weight Watchers, 223-224
  setpoint concept, 65-67
  volunteer agencies, 237-238
Weight loss
  influence of group
    dynamics, 214-224
  maintaining long-term, 12
  and mortality, 9T
  predicting success of, 12
Weight Watchers, 223-224
Whole-body plethysmography, 27

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